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OCULAR MANIFESTATIONS IN HYDROA VACCINIFORME

WILLIAM H. STOKES, M.D.

OMAHA

Hydroa vacciniforme is a disease described in textbooks of dermatology as a recurring vesicular eruption, occurring for the most part in the summer and usually affecting young men. The lesions are seen more commonly on surfaces of the skin exposed to light. The disease has been known by a variety of names. Bazin [1] in 1862 reported the first typical case, calling the condition "hydroa vacciniforme." Hutchinson [2] in 1878 referred to the disease as "prurigo aestivalis," "prurigo adolescentium" and "acne prurigo." Hutchinson, however, did not correlate the condition in his group of cases with that in the case reported by Bazin. Later in 1889 Hutchinson [3] again reported a typical case of hydroa vacciniforme and described the condition as "a recurrent summer eruption" or "summer prurigo." Ehrmann [4] in 1905 suggested the name "dermatolysis photoactinica congenita." This term, however, is not to be confused with epidermolysis bullosa, a cutaneous disease, the ocular lesions of which were described by Cohen and Sulzberger [5] in the March issue of the ARCHIVES for 1935.

The name "hydroa vacciniforme" finds almost universal acceptance in the literature, although the terms "hydroa aestivale" and "hydroa vacciniforme" are sometimes used interchangeably. Senear and Fink [6]

From the Department of Ophthalmology of the University of Nebraska.

1. Bazin, A. P. E.: Leçons théoriques et cliniques sur les affections génériques de la peau, Paris, A. Delahaye, 1862, p. 132.

2. Hutchinson, J.: On Certain Rare Diseases of the Skin, in Lectures on Clinical Surgery, London, J. & A. Churchill, 1878, vol. 1, pt. 1, pp. 126 and 133.

3. Hutchinson, J.: A Case of Summer-Eruption Recurring with Great Severity for Many Years, Tr. Clin. Soc., London 22:80, 1889.

4. Ehrmann, S.: Versuche über Lichtwirkung bei Hydroa aestivalis (Bazin), Sommereruption (Hutchinson), Arch. f. Dermat. u. Syph. 77:163, 1905.

5. Cohen, M., and Sulzberger, M. B.: Essential Shrinkage of Conjunctiva in a Case of Probable Epidermolysis Bullosa Dystrophica, Arch. Ophth. 13:374 (March) 1935.

6. Senear, F. E., and Fink, H. W.: Hydroa Vacciniforme Seu Aestivale, Arch. Dermat. & Syph. 7:145 (Feb.) 1923.

in 1923 classified cases of this disease into two groups on the basis of the cutaneous lesions. Into one they placed those cases in which the cellular reaction was insufficient to produce scar formation; this group was designated as cases of hydroa aestivale. In the second group they placed cases in which scar formation was the distinguishing feature, and for this group the name hydroa vacciniforme seemed more appropriate. There is, however, a close relation between the two groups. Möller,[7] for instance, was able in a series of experiments to produce at will lesions of different degrees of severity simply by varying the time of exposure to ultraviolet rays, these lesions in turn varying from a mild erythema, through Hutchinson's prurigo, to vesicle formation, to vesicobullous hydroa and finally to a true hydroa vacciniforme.

INCIDENCE

Senear and Fink,[6] who presented an excellent review of the cutaneous manifestations of this disease, found that although both males and females were affected, males were more frequently attacked, the ratio being practically 2: 1. The disease usually begins in childhood; it seems to be less severe after the age of puberty, but it can still be active in the third or fourth decade of life. A dark complexion is not absolutely protective, since there are cases reported from South America, Italy and Japan (Garrod[8]). Moreira[9] reported a case in which one parent of the patient was a mulatto. There are, however, no cases reported in the Negro race.

ETIOLOGY

The disease is most active in the summer. In cases in which the cutaneous eruption occurs in winter it is likely to appear when bright sunlight is reflected from snow. For this and other reasons the influence of light has been recognized by all observers, and while it is now established that the actinic rays of the sun are the irritating element, the belief also exists that exceptionally warm or cold winds seem sufficient to cause an outbreak. This is a singular and interesting relation between actinic and thermal wavelengths occurring at opposite ends of the solar spectrum. Anderson[10] in 1898 suggested a possible relation between the excretion of porphyrins and the condition of the skin. Cases which are described in the literature are discussed with respect to the excretion

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7. Möller, M.: Der Einfluss des Lichtes auf die Haut in gesunden und krankhaften Zuständen, Stuttgart, E. Nägele, 1900, p. 85.

8. Garrod, A. E.: Congenital Porphyrinuria, Quart. J. Med. **5**:473, 1936.

9. Moreira, J.: Hydroa Vacciniforme Seu Aestivale, Brit. J. Dermat. **7:** 175, 1895.

10. Anderson, T. M.: Hydroa Aestivale in Two Brothers Complicated with the Presence of Hematoporphyrin in the Urine, Brit. J. Dermat. **10**:1, 1898.

of porphyrins or to photosensitivity or to both phenomena. Summaries in this respect were published by Günther[11] in 1912, Gottron and Ellinger[12] in 1931, Mason, Courville and Ziskind[13] in 1933 and by Mathews[14] in 1937. The last-named author surveyed 57 cases of hydroa vacciniforme that had been described since 1905 and found that only in 32 had an examination for porphyrins been made. In 23 of these cases excretion of porphyrin was increased, but in 9 no increase was noted. Mason and his associates therefore summed up the situation by stating that hydroa vacciniforme can occur without increased excretion of porphyrin and conversely that porphyria does not always produce photosensitivity. A careful review of the experimental side of the question by Blum and Pace[15] in 1937 gives no real support to the hypothesis that the lesions of hydroa vacciniforme result from the direct photosensitizing action of porphyrins.

Heredity seems to be a factor. Anderson's[10] 2 patients were brothers; Ehrmann[4] reported a brother and sister affected; Friede[16] stated that 2 brothers and a sister had hydroa vacciniforme; Borzow[17] cited 2 families, in 1 of which the patients—grandfather, mother, daughter and brother—had the cutaneous lesions of hydroa; and in the other family there were 4 sisters and 1 brother affected. Some subjects have been children of consanguineous parents; among these are the patients in the cases reported by Arzt and Hausmann,[18] Garrod[8] and Borzow.[17]

SYMPTOMS

The eruption on the skin is symmetric and is usually limited to the uncovered parts of the body; the bridge of the nose, the cheeks, the ears and the backs of the hands are the parts most affected. The lesions are often preceded by a sensation of heat or itching after exposure to the sun. The eruption begins as a slight irritation or redness followed by vesicles or bullae, most of which are filled with clear serum while others

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11. Günther, H.: Die Hämatoporphyrie, Deutsches Arch. f. klin. Med. **105:** 89, 1912.

12. Gottron, H., and Ellinger, F.: Beitrag zur Klinik der Porphyrie, Arch. f. Dermat. u. Syph. **164:**11, 1931.

13. Mason, V. R.; Courville, C., and Ziskind, E.: The Porphyrins in Human Disease, Medicine **12:**355, 1933.

14. Mathews, F. P.: Photosensitization and the Photodynamic Diseases of Man and the Lower Animals, Arch. Path. **23:**399 (March) 1937.

15. Blum, H. F., and Pace, N.: Studies of Photosensitization by Porphyrins, Brit. J. Dermat. **49:**465, 1937.

16. Friede, R.: Ueber Hydroa vacciniforme des Auges, Klin. Monatsbl. f. Augenh. **67:**26, 1921.

17. Borzow, M. W.: Drei Fälle von Hydroa vacciniforme mit Erscheinungen seitens der Hypophyse, Arch. f. Dermat. u. Syph. **168:**534, 1933.

18. Arzt, L., and Hausmann, W.: Zur Kenntnis der Hydroa, Strahlentherapie **11:**444, 1920.

are pustular. Central necrosis of the blisters may appear followed by crusting, healing and scar formation. The scars on the face are of the varioliform type, but those on the hands are often slightly raised. At first they are red, but gradually over a period of months they fade and leave permanent scars. Repeated attacks result in cicatrization, mutilation of the parts and loss of substance, especially of the ears, the nose and fingers (Schmidt-La Baume [19] and Vollmer [20]). The exposed portions of the body often become pigmented and the tissue infiltrated and sclerosed. The formation of scars, however, does not protect against the eruption, since new lesions can develop in scar tissue.

The mucous membrane of the mouth has not been exempt. Garrod [8] described a case in which the circumoral area developed into multiple fibromatosis with a tendency toward pedunculation in many of the lesions. Tesseraux [21] in 1931 reported a case in which ulcerative pharyngolaryngitis occurred.

Lesions of the nail beds have been present in cases reported by Schultz,[22] Ehrmann [4] and Arzt and Hausmann.[18] Shedding of the nails from time to time is a common symptom of the disease. Conspicuous deformities of the hands with fixation of joints and atrophy of the terminal phalanges necessitating amputation has been reported by Günther [11] and by Schmidt-La Baume.[19]

Mackey and Garrod [23] in 1922 pointed out that in congenital porphyria and hydroa vacciniforme the teeth are frequently pigmented and coral pink (erythrodontia). In a recent review Garrod [8] gives the results of a ten year follow-up study on 3 patients with congenital porphyria, 1 of whom had stained decidual teeth and also pigmented permanent teeth. Peachey, Dobriner and Strain [24] in 1938 described a similar case in which the teeth were purplish to reddish brown. It has been shown in autopsy material that the bones are similarly pigmented (Schultz,[22] Günther,[11] Hegler, Fränkel and Schumm [25] and Peachey, Dobriner and Strain [24]) by transillumination of the teeth and bones during life.

19. Schmidt-La Baume, F.: Ein besonders excessiver Fall von Hydroa vacciniforme, Arch. f. Dermat. u. Syph. **153**:368, 1927.

20. Vollmer: Hereditäre Syphilis und Hematoporphynuria, Arch. f. Dermat. u. Syph. **65**:221, 1903.

21. Tesseraux: Ueber eine ulzeröse Pharyngo-Laryngitis bei Hydroa vacciniforme, Arch. f. Dermat. u. Syph. **164**:661, 1932.

22. Schultz, T. H.: Ein Fall von Pemphigus leprosus, Inaug. Dissert., Greifswald, 1874; cited by Günther.[11]

23. Mackey, L., and Garrod, A. E.: Congenital Porphyrinuria, Quart. J. Med. **15**:319, 1922.

24. Peachey, C. H.; Dobriner, K., and Strain, W. H.: Hydroa Estivale in Congenital Porphyria, New York State J. Med. **38**:849, 1938.

25. Hegler, C.; Fränkel, E., and Schumm, O.: Zur Lehre von der Haematoporphyria congenita, Deutsche med. Wchnschr. **39**:842, 1913.

LABORATORY FINDINGS

The blood has been investigated, but nothing outstanding has been discovered. Eosinophilia has been recorded in a few instances.

Of the urinary findings, only the presence of porphyrins seems worthy of note.

The porphyrias are characterized by a disturbance of pigment metabolism which leads to the increased excretion of porphyrins in the urine and feces. In cases in which the level of excretion is high, the urine is generally the color of Burgundy wine; occasionally, however, the color of the urine is normal, even though the porphyrin content is high. For several decades the name "hematoporphyria" was used as a nomenclature for the different forms of the disease, even after it was recognized that hematoporphyrin is not present in the excreta (Peachey, Dobriner and Strain [24]). For this reason the name "porphyrinuria" is preferable to that of "hematoporphyrinuria," a term which Hans Günther [11] first introduced.

In many records of cases of hydroa vacciniforme no mention is made of the urine. In some cases no porphyrins were found, but there are only a few cases in which the stools have been examined, so that it is possible that the association of an excessive excretion of porphyrins is more common than statistics would indicate.

DIFFERENTIAL DIAGNOSIS

The character and distribution of the lesions, their occurrence chiefly in spring and summer and the fact that the vast majority of the persons affected are young men should serve to exclude erythema multiforme, pemphigus and dermatitis herpetiformis from hydroa vacciniforme, the only disorders with which the latter is likely to be confused.

TREATMENT

The treatment has been unsatisfactory, and the prognosis is poor as far as the prevention of cutaneous scarring is concerned. The usual form of treatment has been the prescription of topical protective substances, such as salves or dusting powders containing esculin or quinine salts, the object being to exclude ultraviolet rays. A similar result may be obtained by the use of veils and umbrellas. In recent years liver therapy and glandular extracts have been employed (Sellei,[26] Wendeberger and Klein,[27] and Peachey, Dobriner and Strain [24]).

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26. Sellei, J.: Ueber das Entstehen des Hydroa vacciniforme s. aestivale, Arch. f. Dermat. u. Syph. **174**:177, 1936.

27. Wendeberger, J., and Klein, A.: Ueber Hydroa vacciniformis, Arch. f. Dermat. u. Syph. **176**:522, 1938.

HYDROA VACCINIFORME AND THE EYE

Recorded examples of hydroa vacciniforme with ocular complications are few, and most of the patients have been under observation for a relatively short time. Since so little is known in regard to the primary cutaneous disturbance, it follows that knowledge of the ocular manifestations must be much less. Individual reports are somewhat at variance, but by reviewing all the reported cases there may perhaps emerge a better understanding of the pathologic and clinical pictures. To this end therefore I feel justified in presenting this study with the addition of 2 more cases to the present series in the literature. I have been able to discover only 20 instances in which hydroa vacciniforme gave rise to ocular complications. (There are about 100 cases of hydroa vacciniforme recorded.) Of the 20 case reports in which ocular lesions were encountered, 7 were cited by ophthalmologists. The only 2 references found in the American literature were those of Miller[28] and Senear and Fink.[6]

INVOLVEMENT OF THE EYELIDS

The ocular symptoms appear coincidentally with an outbreak of facial blistering, and the eruption on the lids occurs in successive outbreaks, depending on exposure to the sun's rays. The lesions are often preceded by a sensation of heat in the affected part. After the eruption is once established, the patient may suffer itching and occasionally pain, but quite as frequently he does not complain of any symptoms. In a number of cases the attacks have been ushered in by some general symptoms, such as chills and nausea, malaise and a slight rise in temperature (Möller,[7] Günther[11] and Halberstädter[29]). The first cutaneous lesions to appear are red macules, which rapidly become transformed into vesicles or bullae, occurring either singly or in groups simulating herpes. These vesicles may dry in a few days, or they may rupture and form a crust. Many of the larger vesicles become depressed in the center and become darker in color. Surrounding the vesicle there is a reddened areola. The dark center is converted into a thick adherent crust, which on falling leaves a depressed reddened scar that eventually becomes white. With the acute symptoms there is at times a marked edema of the lids with a generalized reddening of the skin (Scholtz[30] and Tesseraux[21]).

The resulting scarring of the lids may lead to the formation of ectropion (Möller,[7] Wendeberger and Klein[27] and Friede[16]). Atrophic

28. Miller, E. B.: Manifestations of Hydroa Vacciniforme, Tr. Coll. Physicians, Philadelphia **45**:384, 1923.

29. Halberstädter: Hydroa aestivale, Arch. f. Dermat. u. Syph. **79**:465, 1906.

30. Scholtz: Beitrag zur Lehre von der Hydroa aestivalis, Arch. f. Dermat. u. Syph. **85**:95, 1907.

changes of the skin may lead to marked shrinkage, tightening and stiffening of the upper and lower lids, which renders them almost immobile and causes a narrowing of the palpebral fissure (Vollmer,[20] Linser [31] and Schmidt-La Baume [19]). The entire loss of both eyelashes and eyebrows has been reported (Schmidt-La Baume [19]).

Bilateral exophthalmos with marked orbital cellulitis and fixation of both globes is described (Friede [16]). Exophthalmos has been reported associated with a symmetric necrosis of the temporal side of both sclera, but it disappeared after the eyes were covered with a dark bandage.

INVOLVEMENT OF THE CONJUNCTIVA AND SCLERA

A severe conjunctivitis may occur with or without the appearance of vesicles on the conjunctiva, alone or in association with keratitis (Möller,[7] Halberstädter,[29] Scholtz [30] and Tesseraux [21]). This conjunctivitis is often of the congestive type, with edema and chemosis, associated with lacrimation, photophobia and blepharospasm (Möller,[7] Scholtz [30] and Miller [28]). There may be an outbreak of vesicles on the conjunctiva (Urbanek [32]) with erosion and necrosis of the conjunctival tissue. Later, atrophy of the conjunctiva may take place with scar formation, binding the conjunctiva firmly to the sclera (Kuhnt [33] and Friede [16]). The ulcerating necrosing process may affect the sclera (Zinsser,[34] Günther [11] and Kreibich [35]). The ulceration is often bilateral and affects the temporal surfaces of the sclera more often than the nasal surfaces. The lesion is circumscribed and has a punched-out appearance; the uveal pigment can be seen shining through the crater of the ulcer, and the eye becomes staphylomatous (Kuhnt [33] and Friede [16]). In the case reported by Kuhnt secondary glaucoma developed for which an iridectomy became necessary. The vesicular eruption sometimes appears on the conjunctiva and cornea, most typically at the limbus, where it resembles phlyctenular conjunctivitis and keratitis with indolent ulcers (Scholtz,[30] Kuhnt,[33] Zinsser [34] and Miller [28]).

A peculiar hypertrophy of the conjunctiva at the limbus has been reported which bears a marked resemblance to the bulbar type of spring

31. Linser, P.: Ueber den Zusammenhang zwischen Hydroa aestivale und Haematoporphyrinurie, Arch. f. Dermat. u. Syph. **79**:251, 1906.

32. Urbanek, J.: Lichtdermatitis und eine Lichterkrankung der Konjunktiva, Ztschr. f. Augenh. **61**:66, 1927.

33. Kuhnt, H.: Ueber symmetrische umschriebene Skleralnekrose bei Hydroa vacciniforme, Ztschr. f. Augenh. **27**:146, 1912.

34. Zinsser, F.: Hautkrankheiten und Mundschleimhaut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 14, pt. 1.

35. Kreibich, K.: Ueber Hydroa vacciniforme und Frühjahrskatarrh, Wien. klin. Wchnschr. **20**:1286, 1907.

catarrh or vernal conjunctivitis (Kreibich,[36] Urbanek,[32] Gottron and Ellinger,[12] and Bezecny and Bieringer[37]). The granulations near the limbus consisted of pale, yellowish-brownish or grayish raised gelatinous tissue, and in this region the characteristic vascularization was evident, the same as one sees in cases of spring catarrh. There was a milky discoloration of the conjunctiva of the tarsus, but cobble-stone granulations of the tarsal conjunctiva have not been reported by any of the observers.

It is of interest to note that the 3 cases reported by Kreibich[36a] were also observed by Müller and Dimmer, of Vienna, and the presumptive diagnosis of the limbic form of vernal conjunctivitis and hydroa vacciniforme was substantiated. The limbic lesions cleared up within a month when the eyes were covered but recurred when the bandages were removed. Gelatinous hypertrophic tissue near the limbus was also described by Bezecny and Bieringer,[37] and in his case cystic degeneration was noted in the raised masses. This is the only example in the literature in which biopsy material was examined microscopically. The tissue resembled and also showed the microscopic changes described in vernal conjunctivitis.

INVOLVEMENT OF THE CORNEA

Corneal complications are due either to the results of the vesicle formation on the cornea (Plöger,[38] Ledermann[39] and Friede[16]) or may be secondary to the complications of the lids, where there is an ectropion (Möller[7]). In the patients reported by Kuhnt[33] and Friede[16] the corneal involvement was noted to be present only on the exposed surfaces of the cornea, while the upper covered portion of the cornea remained perfectly clear. Vesicle formation occurred, the epithelium being raised in tiny blisters, and these, when they broke, left denuded areas. Sometimes the cornea healed and remained clear; more often deep ulcers formed, the cornea became infiltrated and a superficial keratitis with vascularization resulted. Friede[16] reported a sclerosing keratitis. Opacities up to the stage of complete leukomas were seen by Ledermann,[39] Kreibich,[35] Scholtz,[30] Plöger,[38] Günther,[11] Kuhnt[33] and Garrod.[8] In Kuhnt's patient an adherent leukoma developed with secondary glaucoma which had to be relieved by iridectomy.

36. Kreibich, K.: (*a*) Zur Wirkung des Sonnenlichtes auf Haut und Konjunctiva, Wien. klin. Wchnschr. **17**:673, 1904; (*b*) footnote 35.

37. Bezecny, R., and Bieringer, S.: Zur Histologie der konjunktivalen Erkrankung bei der Sommerprurigo, Klin. Monatsbl. f. Augenh. **91**:810, 1933.

38. Plöger: Hydroa vacciniformis, Sitzungsh. d. ärztl. Ver. München **5**:28, 1910; abstracted, München. med. Wchnschr. **57**:1475, 1910.

39. Ledermann: Hydroa vacciniformis, Dermat. Ztschr. **6**:368, 1899.

Decreased sensitivity (anesthesia) of the cornea and conjunctiva is mentioned by Kuhnt[33] and Friede,[16] and this in eyes with low intra-ocular tension.

OPHTHALMOSCOPIC AND VISUAL FIELD CHANGES

Ophthalmoscopic changes are described by Friede.[16] His patient had bilateral atrophy of the optic nerve of moderate degree as a result of intense and prolonged orbital cellulitis. The visual fields of this patient showed a moderate concentric contraction for form and colors associated with a bilateral ring scotoma. An absolute central scotoma was present in one eye. Changes in the visual field are also reported by Kuhnt[33] as a bilateral concentric contraction for form and color.

Borzow[17] discussed 3 interesting patients with pituitary dysfunction discovered by roentgen examination and subsequent functional tests, 2 of whom had a bitemporal hemianopia; all had the characteristic lesions of hydroa vacciniforme.

REVISIONS IN THE ORIGINAL DIAGNOSIS

The association of hydroa vacciniforme and porphyrinuria with ocular complications has been met with, and it is probable that this association was exemplified in 2 cases of earlier date, the 1 recorded by Schultz[22] in 1874 and the other by Nebelthau[40] in 1899 and again by Vollmer[20] in 1903, although their inclusion in the list must of necessity involve a revision of the original diagnosis.

Schultz's patient was a man aged 33, whose condition was diagnosed with hesitation as leprae bullosa and from whose red urine two abnormal pigments were obtained, one of which was undoubtedly a porphyrin. The description of the cutaneous lesions and of the scarring and mutilations to which they gave rise justifies a revised diagnosis of hydroa vacciniforme.

Nebelthau's,[40] and later Vollmer's,[20] patient was a woman aged 45, who dated her cutaneous disease from the first year of her life and had passed red urine as long as she could remember. The cutaneous lesions were described as being due to congenital syphilis by a process of exclusion, but actually they resembled in all respects those which result from hydroa vacciniforme. The sclerotics had been attacked; there was scarring on the face and hands and the usual mutilations of the ears and nose. Hans Fischer[41] stated later that the patient, who had then become blind, died at the age of 65. Interestingly enough, one of her relatives (Schmidt-La Baume[19]) suffered from hydroa vacciniforme.

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40. Nebelthau: Beitrag zur Lehre vom Haematoporphyrin des Harns, Ztschr. f. physiol. Chem. **27:**324, 1899.
41. Fisher, H., cited by Mackey and Garrod.[23]

REPORT OF CASES [42]

CASE 1.—*History.*—A. W., aged 33, an American-born Iowa farmer, complained of an eruption on his face, wrist and back of his hands. The eruption had been present during the warmer months for twenty years, first appearing at the age of 13. It usually began in early April and lasted until November, sometimes longer. On several occasions the eruption had appeared in winter after exposure to sunlight, when there was snow on the ground. The chief symptoms were burning and pain in the involved areas. The patient was in good health otherwise, except for an obstinate constipation, for which he took proprietary cathartics regularly. The family history disclosed a brother and 2 sisters, neither of whom had had any similar trouble, nor was there any knowledge of a cutaneous disease in the ancestors.

Examination.—On the nose, lips and cheeks, chin, ears and exposed area of the neck were many superficial round or gyrate (grouped) crusted erosions, indicative of a primarily vesicular eruption (fig. 1). The crusts were serosanguineous and seropurulent and firmly adherent. There was a narrow areola of erythema about each crust. In these areas, between the crusts were many atrophic scars, apparently from previously healed similar lesions. On the dorsa of the hands and about the exposed areas of the wrists were about twenty vesiculopustular lesions varying in size from that of a wheat kernel to that of a large pea and in various stages of evolution; there were also several depressed scars. The lesions which were apparently fully developed had a dark brownish black depressed center, a tense raised pustular ring about this center and a bright inflammatory areola, as seen in the lesions of vaccinia. Otherwise general examination gave negative results except for an inflammatory process on the left conjunctiva and cornea.

There were no stigmas of congenital syphilis. The Wassermann reaction of the blood was negative. The results of routine urinalysis and blood counts were negative. (Metabolic studies and porphyrins will be reported elsewhere by Dr. Cameron.)

The patient was seen again during the midsummer and had at that time made no improvement under therapy, including the administration of hydrochloric acid by mouth and a trial of the following ointments: 4 per cent ammoniated mercury in zinc oxide ointment, 5 per cent disodium naphthol sulfonate in petrolatum and 10 per cent lampblack in petrolatum.

The dermatologic diagnosis was hydroa vacciniforme.

Ophthalmologic Report (April 9, 1934).—The patient complained of photophobia and lacrimation, especially of the left eye. Pain had been present a month previously, when the symptoms first appeared, but for the past two weeks the pain had not been severe. However, the patient felt that he wanted to keep his eyes closed. His eyes had been inflamed on previous occasions, especially the previous summer when he noticed some clouding of his vision, associated with photophobia and lacrimation. These symptoms were relieved considerably at the time by wearing dark glasses. On his left eye he had noticed a small growth which had been present for the past three years.

External Examination: Vision of the right eye was 20/25. There were a few small scars on the surface of the skin of the lower lid of this eye. The conjunctiva was somewhat congested and slightly edematous, especially on the

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42. The patients in the 2 cases reported were referred by Dr. Olin J. Cameron, Omaha, a dermatologist.

exposed surface and near the limbus. The cornea seemed to be clear; there were no scars or visible ulcerations. Vision of the left eye was 20/100. Near the limbus on the temporal surface of this eye there was an overgrowth of connective tissue with hypertrophy of the conjunctiva. The tissue in this area was thickened, and the interpalpebral area near the limbus consisted of grayish-reddish nodules, some of which had a gelatinous appearance. This hypertrophic tissue was markedly vascular. The cornea showed a diffuse clouding and an ulcer about 2 mm. from the limbus at 7 o'clock. This denuded area was triangular, with rounded contours, and measured about 2 mm. in circumference. Considerable circumcorneal congestion was present. Both corneas showed a definite hypesthesia noted by esthesiometric tests with Frey hairs.

Fig. 1 (case 1).—Patient with hydroa vacciniforme. The photograph shows the vesicular eruption on the nose, lips, cheeks, ears and exposed area of the neck and also on the dorsa of the hands and on the exposed areas of the wrist.

Slit Lamp Examination: After instillation of fluorescein the corneas were examined with slit lamp corneal microscope. Although the cornea of the right eye appeared prefectly normal to ordinary examination, it later showed a picture almost identical with a superficial type of punctate keratitis. Small staining areas were noticed, mostly over the central and exposed surface of the cornea. Tiny droplets were present; these were seen also with retroillumination. The droplets collected apparently between the epithelial cells and in numerous places formed small confluent blebs. Besides these staining areas there were noted many white dots which did not stain with fluorescein, these dots apparently representing the sites of former blebs. The corneal nerves appeared swollen. On being stained with fluorescein the left eye showed a rather large circumscribed epithelial defect

in the area which had been previously described as an ulcer. Apparently this exfoliation of the epithelium was the result of vesiculation. Multiple epithelial defects were seen in other portions of the exposed surface of the cornea. The cornea showed edema, appearing like glass which had lost its polish. A number of small coalescing epithelial bullae were also found. There were many small dots which did not stain and marked the sites of former blebs. The anterior chamber showed a few cells. The conjunctiva had a gelatinous appearance, especially near the limbus; the surface was uneven, and numerous elevated vesicles were seen situated apparently in the subepithelium. The capillaries in this area were markedly dilated and tortuous.

Microscopic Examination.— A small piece of conjunctival tissue was removed from the neighborhood of the limbus for microscopic study and showed the

Fig. 2 (case 1).—Section of conjunctiva. There is vesicle formation characterized by subepithelial fissuring. The connective tissue is edematous and shows a diffuse round cell infiltration with monocytes, lymphocytes and polymorphonuclear cells, most of them showing signs of necrosis. The blood vessels are dilated. Hematoxylin and eosin stain; × 140.

following changes: The epithelium of the conjunctiva did not appear to be even and regular. In some places the epithelial layer seemed absent. In other areas there was a tendency to vesicle formation, characterized by subepithelial fissuring (fig. 2). Here the subepithelial connective tissue was edematous, and there was a diffuse cellular infiltration. This tissue showed many monocytes, lymphocytes and polymorphonuclear cells, most of them showing signs of necrosis. The blood vessels in this neighborhood seemed markedly dilated. Some of the leukocytes in the subepithelial edematous tissue appeared to be eosinophils, but they were proportionately less numerous in the tissues than in the capillaries lying beneath the epithelium. Examination of the conjunctival secretion revealed no evidence of eosinophils.

The surface epithelium of the conjunctiva showed keratinization. In other areas there seemed to be a tendency toward marked hypertrophy, causing the epithelium to be thickened. The most characteristic feature of this overgrowth was the ingrowth of solid rods and processes of epithelium into the underlying fibrous tissue (fig. 3). There was a tendency for these subepithelial overgrowths to become folded, forming epithelial cysts and subepithelial cell nests (fig. 4). The basement membrane, however, was always intact. Associated with this overgrowth of epithelium was a marked fibrosis of the conjunctival connective tissue, and in the deeper zones the walls of blood vessels appeared markedly thickened.

Treatment of Corneal Lesion.—The corneal lesions healed promptly in four days after both eyes were covered with a protective dressing. An ointment containing mercury bichloride (1 : 3,000) was placed in the conjunctival cul-de-sac

Fig. 3 (case 1).—Section of conjunctiva. The epithelium of the conjunctiva shows keratinization. There are marked overgrowth and ingrowth of solid rods and processes of epithelium into the underlying fibrous tissue. The conjunctival tissue shows marked fibrosis. Hematoxylin and eosin stain; × 140.

once daily. No staining of the cornea of either eye was noted on the fifth day. The patient was advised to wear shaded glasses for protection.

Follow-Up Record (Sept. 8, 1939).—The patient has not been seen for five years. During the past three years the lesions on his face have much improved. Although there was extensive scar tissue formation on the exposed surface of the body, there have been no fresh lesions during the past two summers. He has been particularly careful about his eyes by not working in the heat of the sun, and he has always worn protective glasses when out of doors. However, there were times when his eyes were irritated, but he was able to alleviate the irritation by staying indoors.

Examination of his eyes at this time showed his vision to be 20/20 in both eyes. On the left cornea there was a small nebulous opacity about 2 mm. from

the limbus, not interfering with the pupillary area of the cornea. Both corneas, however, still showed a definite hypesthesia. Staining of the cornea with fluorescein revealed small punctate staining areas on the exposed surfaces of each cornea when examined with the corneal microscope. The examination showed the fundus to be normal, and the visual fields showed no abnormality.

CASE 2.—*History.*—S. D., an otherwise healthy blonde, American-born girl 6 years of age, had been under the care of Dr. Olin Cameron for the previous two years for an eruption involving her face and the backs of both hands. This eruption usually made its appearance in May and continued unabated until the early winter, disappearing at the time of frost. The lesions were described by the parents as "pus-pimples, leaving holes in the skin which bleed." Healing occurred with scar formation. More correctly the lesions consisted of several shotty papulopustules on the forehead and temples; in this location as well as on the
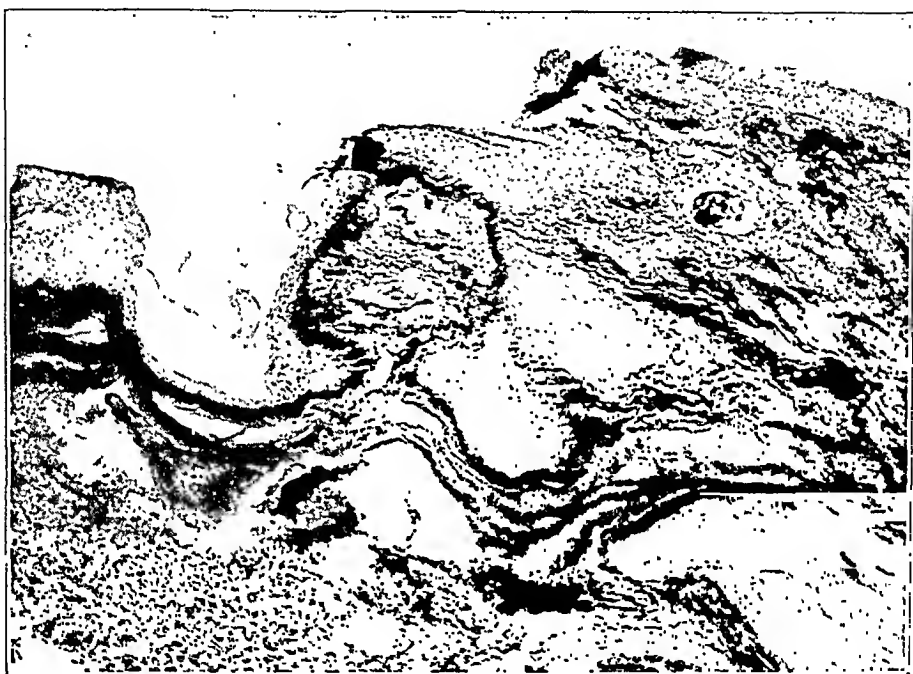
Fig. 4 (case 1).—Section of conjunctiva. The subepithelial overgrowths have become folded, forming epithelial cysts and subepithelial cell nests. Weigert's picrofuchsin stain; × 78.

upper lids, cheeks and dorsal surfaces of both hands there were also present a number of atrophic scars. When she was to be out in the sun the parents had been instructed to apply a protective ointment of 10 per cent disodium naphthol sulfonate to the face and hands, and other precautionary methods were instituted for the treatment of hydroa vacciniforme, as suggested by Dr. Cameron.

Ocular Examination (June 20, 1939).—The parents have never noticed any ocular complications. The eyes at times were a little red and watery when the child played out of doors, but she never complained.

Vision was 20/20 in both eyes, and the external ocular structures were normal. The child did not complain of a burning sensation in her eyes after instillation of a solution of fluorescein, and from this test it was assumed that a

hypesthesia existed. The surface of the cornea in each eye as viewed with the corneal microscope and slit lamp showed a few small round staining areas resembling the lesions of superficial punctate keratitis. The conjunctiva of the globe appeared normal.

SUMMARY

Hydroa vacciniforme is a disease which should be of interest to the student of genetics, to the biochemist and to the clinician as an example of a constitutional peculiarity which renders the patient susceptible to external influences that are harmless to average persons—in this instance a disease provoked by exposure to sunlight.

A review is made of previously reported ocular complications in cases of hydroa vacciniforme.

The corneal complications as seen with the slit lamp and corneal microscope in 2 patients are reported.

A report is made on a section of conjunctivas removed for microscopic study.

MEASUREMENT OF THE STRUCTURES OF THE FUNDUS

PRESENTATION OF AN IMPROVED TECHNIC

JOHN M. COTTON, M.D.*

AND

SEYMOUR ROSIN, PH.D.

NEW YORK

This communication presents a method for making measurements on the fundus of the eye with a degree of accuracy never before obtained. The heliometer eyepiece for the Gullstrand ophthalmoscope, constructed by Lobeck in 1935, introduced a technical refinement that has made such accuracy feasible. However, with the original method of use as described by Lobeck the possible error of any individual measurement was as great as with many previous methods that have been discarded. With the application of the method introduced in this paper, measurements with the Lobeck eyepiece may be corrected to an accuracy of 0.01 mm.

The development of the ophthalmoscope in the middle of the last century opened a new avenue for the study of the living human body. The advantage of such a direct method of examination for the investigation of local conditions in the eye is obvious, but it was recognized early that this procedure was of much wider usefulness. The presence of the optic nerve in the ophthalmoscopic field allows a close clinical approximation of cerebrospinal fluid pressure within the central nervous system. The presence of the vascular system of the eye in the visualized area offers the only opportunity of studying the arterial, venous and precapillary system of a total organ under normal physiologic conditions. This allows close clinical approximation of the status of the vascular tree of the brain, for, anatomically and physiologically, the vessels of the brain and of the eye are quite similar. Of even wider importance is the fact that systemic disturbances of the circulatory apparatus, such as nephrosclerosis, arteriosclerosis and hypertension, are represented by characteristic changes in the arterial and arteriolar structures of the eye.

In estimating the size of structures of the fundus it has been the usual procedure in clinical practice to relate the object to be measured to the diameter of the papilla, since this is a constantly available large structure on the background of the eye and it has been thought to vary little in diameter from person to person. However, any such approximation must necessarily be very gross, and when one is dealing with structures as small as the retinal vessels or lesions of the choroid and retina, changes imperceptible by such a method may be of utmost diagnostic or prognostic significance.

There have been many attempts at accurate measurement of these structures, but the difficulties inherent in the problem have either prevented reasonable accuracy or have made accurate measurement so complex that it was of no practical clinical value. Methods have been developed during the past few years that have tried to supply the clinician with a simple, accurate technic, but, as it will be pointed out later, each method has failed.

The method presented in this paper is of double importance, for it can be used not only as a simple clinical procedure but for fine determinations of value to the research scientist. The clinician may make measurements of reasonable clinical accuracy that will allow the evaluation of heretofore imperceptible extensions or regressions of retinal lesions in less than five minutes. A slightly longer period is necessary for exact measurements, but the figures thus obtained are of sufficient accuracy to allow reliable interpersonal comparisons of differences as small as 0.01 mm.

HISTORY

The first record of an attempt to measure objects on the background of the eye was published shortly after Helmholtz [1] announced the discovery of the ophthalmoscope in 1851. In 1852 Ruete [2] described a method whereby a scale was projected into the examining eye to overlay the virtual image of the fundus of the examined eye. Measurements of the structure being studied were made relative to the observed diameter of the optic nerve head. Two years later Ruete announced another method [3] for making measurements on the reversed image. He projected the image into a blackened tube containing a plane mirror on which was etched a millimeter scale.

In 1854 Donders [4] constructed a special ophthalmoscope, which differed from the earlier instruments in that the shadows of the measuring

1. Helmholtz, H. L. F.: Beschreibung eines Aûgen-Spiegels zur Untersuchung der Netzhaut im lebenden Auge, Berlin, A. Förstner, 1851.

2. Ruete, C. G. T.: Der Augenspiegel und das Optometer für practische Ärzte, Göttingen, Dieterich, 1854.

3. Ruete, C. G. T., in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1920, vol. 1, p. 319.

4. Donders, F. C.: Lehrbuch der Ophthalmologie, Brunswick, 1854.

scale were projected into the examined eye. This ophthalmoscope consisted of a square box containing a diagonally placed perforated mirror. There were projections from opposite sides of the box for the eye of the patient and for the examiner. On a third side of the square box was located the light source, which was carried through a blackened tube to be reflected by the perforated mirror into the eye of the patient. In the proximal end of the tube that transmitted the light source were located two movable arrows pointed at one another, lying in a diameter of the tube. The shadows of these arrows were projected on the background of the examined eye and measurements made by adjusting the points of the arrowheads, by means of a micrometer, to coincide with the margins of the structure to be measured. In order to make measurements with any accuracy, the eye of the patient must be exactly accommodated to the arrowheads so that the image on the retina is sharp.

In 1857 Schneller,[5] working with rabbits, devised another method for measuring the real image. He fastened long parallel rods to the frame surrounding the condensing lens that he used to form the image. These rods were supported at the other end by a similar frame without a lens. At the point where the reversed image might be expected, he perforated the rods with pointed screws and measured the distance between points on the image by adjusting the screws. This method requires sharp focusing, and the measuring screws must be exactly in the line of the image. The author stated that there were many technical difficulties in the method.

Landolt [6] in 1878 introduced a modification of the original method of Ruete. A small plane mirror with the center free from silver was fastened to the back of the mirror of the ophthalmoscope. This mirror was fastened on a small rod that was connected to the ophthalmoscope by means of metal loops, in which it was freely movable about an axis parallel to the main mirror of the ophthalmoscope. The lower end of the rod was bent at right angles at a point situated beneath the thumb of the examiner in order that he might turn the mirror from side to side with a slight pressure. This mirror reflected a millimeter grid system into the eye of the examiner that was placed behind him and to one side. The reflection of the millimeter grid system was superimposed on the virtual image of the examined fundus in the eye of the examiner. Measurements of small structures in units of the grid system

5. Schneller: Ein Mikrometer am Augenspiegel und damit ausgeführte Untersuchungen über den Einfluss bestimmter Eingriffe auf die Circulation in den Augen lebender Kaninchen, Arch. f. Ophth. (pt. 2) **3**:121, 1857.

6. Landolt, E.: Mikrometrie des Augenhintergrundes, in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1920, vol. 1, pt. 2, p. 271.

were made relative to the diameter of the papilla, or exact measurements to 0.1 mm. could be made by using the elaborate formulas furnished by Landolt.

Bretagne [7] and Dufour [8] in 1926 introduced the idea of etching a micrometer grid scale on the objective lens of the ophthalmoscope. This scale was superimposed on the image of the fundus in much the same way as that of Landolt's, and measurements were calculated from the readings by appropriate formulas. There have been modifications of this technic in recent years, all based on the same general plan of etching a scale on the lens of the ophthalmoscope to overlay the image of the fundus.[9] Probably the most refined modification is that recently reported by Neame,[10] in which there is not only a grid system but accurately etched lines of varying width for measuring finer structures.

In 1924 Henrikson [11] measured structures on the background of the eye, making use of the heliometer principle. This is the principle of measuring by moving two lens halves that are divided by a meridional section through the optic midpoint. This method, also called the doubling principle, has been used in astronomic telescopes for over one hundred years. In the first models it was the objective lens that was divided. In 1843 Steinheil, at the instigation of Spruve, constructed an ocular heliometer according to the same principle; Browning constructed still another ocular type in 1872. Following the same principle, Goldmann constructed a measuring ocular for the corneal microscope in the slit lamp.[12]

Henrikson, in making use of the heliometer principle, cut the objective lens on the Gullstrand ophthalmoscope and calculated the size of the structures on the fundus from the amount of movement of the divided lens halves necessary for determination of the size of the structures in the image of the eyegrounds.

In 1931 Nordensen [13] made measurements of the fundus from photographs of the background of the eye, made with the Nordensen camera.

7. Bretagne, P.: Loup ophthalmoscopique micrométrique, Ann. d'ocul. **163**: 192, 1926.

8. Dufour: La mensuration des détails du fond de l'oeil, Ann. d'ocul. **163**: 198, 1926.

9. Spinelli, F.: Mikrometrie des Augenhintergrundes, Klin. Monatsbl. f. Augenh. **92**:93, 1934.

10. Neame, H.: Method of Estimating the Caliber of Retinal Arteries by Means of an Ophthalmoscope, Tr. Ophth. Soc. U. Kingdom **56**:155, 1936.

11. Henrikson, V.: An Investigation on the Measurement of the Eye, Hygiea **86**:887, 1924.

12. Goldmann, H.: Ein neues Messokular für die Spaltlampe, Klin. Monatsbl. f. Augenh. **88**:818, 1932.

13. Nordensen, J. W.: Ueber Messungen am Augenhintergrunde, Ztschr. f. ophth. Optik. **19**:1, 1931.

He used one-hundredth of the diameter of the papilla as the unit of measurement, so all measurements were necessarily relative to this structure. Tengroth [14] and Dimmer [15] also reported on the use of this method. In addition, Nordensen described a method for making measurements on the fundus in the sagittal dimension by using stereoscopic photographs and measuring the parallax, again in terms of some constant on the fundus, usually the diameter of the disk.

The mere fact that there have been so many methods offered without wide acceptance of any one is strong evidence of the limations of each. The methods of Ruete, Donders, Schneller, Landolt, Bretagne, Spinelli and Neame all depend on projecting the inverted image on a scale or projecting a scale into the eye on the upright image. Besides the practical difficulties of each method, they all have in common one serious technical disadvantage, i. e., that it is impossible to focus on both end points of an object on the fundus of a living moving eye and to measure these points on a scale, because as soon as the examiner starts to focus on one end point, the other may have changed its position due to movements of the eye of the patient or the examiner.

The principal disadvantage of the Nordensen method is that it is necessary to have very sharp photographs. In order to make accurate measurements, the photographs must be magnified, and the great difficulty of getting pictures sufficiently sharp to allow magnification is well known to any one with experience with the Nordensen camera. Also, it is necessary for the position of the eye to be the same in relation to the optical system of the camera and the ophthalmoscope for any two plates to be comparable.

Henrikson's method, using the doubling or heliometer principle, was a distinct advance except for one serious technical disadvantage. Since the light from the ophthalmoscope must pass through the objective lens, any movement of that lens must necessarily move the light being projected into the eye. With a lens of the usual focal length, this movement is so great that it is impossible to measure structures as large as the papilla because the displacement required throws the light outside the pupil. When a lens of the proper focal length to allow measurement of the papilla is substituted, the magnification is so small as to preclude accurate measurements of the vessels.

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14. Tengroth, S.: Demonstration of Measurements of the Fundus of the Eye, Hygiea **92**:828, 1930.

15. Dimmer, F.: Die Macula lutea des menschlichen Netzhaut und die durch sie bedingten entoptischen Erscheinungen, Klin. Monatsbl. f. Augenh. **45**:296, 1907.

METHOD EMPLOYING THE LOBECK EYEPIECE

In 1935 Lobeck[16] described a method for making measurements on the fundus, using the standard monocular Gullstrand ophthalmoscope with an especially constructed ocular that makes use of the heliometer principle. The basic principles of the instrument[17] are essentially similar to those of the Henrikson apparatus. However, the ocular devised by Lobeck removes all the disadvantages of the Henrikson method. Since the light does not pass through the ocular, it is undisturbed during measurements of any size. The ocular is freely movable around the optic axis of the instrument, and thus the line of division between the two lens halves may be turned to any angle, decreasing the difficulty in fixation so prominent with the Henrikson method. The Lobeck ocular is equipped with a micrometer graduation in divisions of 0.01 mm.[18]

Fig. 1.—Measurement of the disk by the heliometer method.

The method of using the Lobeck ocular is simple. The patient is seated before the ophthalmoscope with the head supported in an ordinary chin rest. The eye is fixed by directing the patient to focus on a small movable fixation point. As soon as the retina is clearly visualized, the papilla is brought into the center of the field by adjusting the fixation point. The ocular is set so that the dividing line between the lens halves is exactly horizontal. The measurement of the horizontal diameter of the papilla is made by turning the micrometer screw until the papilla has been exactly displaced on itself (fig. 1).

16. Lobeck, E.: Ueber Messungen am Augenhintergrunde, Arch. f. Ophth. **133**:153, 1935; Ueber den Durchmesser der Netzhautgefässe am gesunden und kranken Menschen, ibid. **136**:439, 1937.

17. The Lobeck eyepiece is manufactured and distributed by Carl Zeiss, Inc.

18. In order to construct the ocular so that both half images are exactly and sharply separated and more exact measurements made, a double prism is placed between the collecting lens and the cut lens of the ocular. The prism is so placed that the refracting edge lies exactly in the optic plane of the line of division of the cut lens near the eye.

In measuring vessels it is necessary that measurements be made perpendicular to the course of the vessel. This is accomplished by turning the ocular until the line of division between the lens halves is exactly perpendicular to the course of the vessel. The vessels should always be measured at a constant point so that proper reference can be made. The only constant point in the eye in relation to all vessels is the margin of the disk, so that point has been chosen by most authors. In order to bring this particular point to the measuring line, it is necessary to move the eyes lightly, and this is accomplished by small movements of the fixation point. When this has been accomplished the measurement is made in the same manner as with the disk (fig. 2).

In the original method described by Lobeck and used by Kühn [19] and Badtke [20] all measurements of vessels were made relative to the diameter of the papilla. Although the micrometer in the ocular measures accurately, the image it measures varies with the individual optical system,
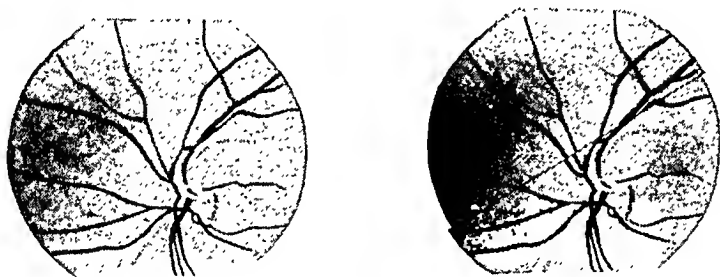
Fig. 2.—Measurement of the vein by the heliometer method.

and thus the measurements do not reflect the actual size of structures on the fundus. In order to convert this relative figure into actual measurements of the structures on the fundus, Lobeck assumed that the papilla has a constant horizontal diameter of 1.5 mm. and used the coefficient of magnification derived by comparing the observed diameter with this constant, to correct his vascular measurements.

The constant of 1.5 mm. for the horizontal diameter of the optic nerve head has been used before in similar situations. It has been impossible to verify the source of this figure, though it is frequently said to be an average value. Eifler [21] reported 1.7 as the average diameter of the nerve. Von Graefe [22] reported an average value of

19. Kühn, W.: Ueber Messungen am Augenhintergrunde, Arch. f. Ophth. **138**:129, 1937.

20. Badtke, G.: Kalibermessungen an den Netzhautgefässen bei Hochdruck- und Nierenkranken, Klin. Monatsbl. f. Augenh. **99**:655, 1937.

21. Eifler, P., in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 1, p. 144.

22. von Graefe, A., in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1910, vol. 1, pt. 2, p. 63.

1.6, varying between 1.5 and 1.7 mm. In our series of 57 measurements made by the more exact method described here, the horizontal diameter of the papilla varied between 1.21 and 1.70 mm., the average being 1.43.[23]

We wished to make comparative measurements between groups of subjects, and when an accepted constant varies so widely in the group the measurements permit little comparison or statistical analysis. However, they would be quite significant if one compared the change in size of a vessel or a lesion in the same person at different times. This is the problem that usually confronts the clinician, and such determinations can be made in a few minutes, without elaborate corrections for the individual refractive error.

There are many situations, however, in which accurate measurements on the fundus are desirable. We frequently wish to compare the size of a structure of the fundus to an accepted norm or to compare retinal changes in groups of subjects with diseases such as hypertension and nephritis, that produce pathologic variations in these structures. Such comparisons are possible only with measurements that rule out the optical factors which are variable in different persons.

Accurate measurement on the fundus is a complex problem because of the wide variation of the optical properties of the individual eye. The method must consider individual variations in refraction and also the optical properties of the measuring instrument. The image presented to the measuring ocular is modified by the media of the eye and the optical system of the ophthalmoscope. Any attempt to derive a coefficient of magnification for each eye measured must take into account all these factors.

MAGNIFICATION FORMULA

The following magnification formula was derived for the Gullstrand ophthalmoscope:

$$Y_R = -\left[\frac{(F_1 + F_2 - CF_1F_2) + b\bar{A}(F_1 + F_2 - CF_1F_2) - \bar{A}(1 - CF_2)}{A + F}\right] \cdot Y_e$$

in which Y_R is the actual size of the retinal object being measured (in millimeters) ; Y_e, the size of the image measured by the measuring eyepiece (mm.) ; F_1, the refracting power of the condensing lens of the ophthalmoscope (in diopters) ; F_2, the refracting power of the collecting lens of the ophthalmoscope (in diopters) ; C, the distance (in meters) between the two fixed lenses or, more accurately, the distance between the second principal point of the first lens and the first principal point of the second lens ; b, the distance (in meters) between the eye and the condensing lens or, more accurately, between the principal point of the eye, located in the aqueous 1.6 mm. from the corneal vertex, and the first principal point of the lens ; $\bar{A}$, the static refraction of the eye (in diop-

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23. Unpublished data.

ters), i. e., the reciprocal of the distance between the principal point of the eye and the far point (it is negative for the myope and positive for the hyperope), and $\bar{F}$, the refracting power of the eye, normally 58.6 diopters, even in cases of ametropia.[24]

That part of the formula immediately preceding Y_e may be considered the coefficient of magnification of the image. If the settings of the instrument are kept constant, then the only variables are b, the distance between the examined eye and the ophthalmoscope, and $\bar{A}$, the refractive error of the examined eye. The distance between the patient's eye and the condensing lens of the ophthalmoscope is kept constant in a simple manner. The distance is adjusted until the light spot on the cornea is the smallest image formed by the condensing lens. Slight movements of the patient's head during the examination can be quickly corrected for by adjusting the position of the ophthalmoscope.
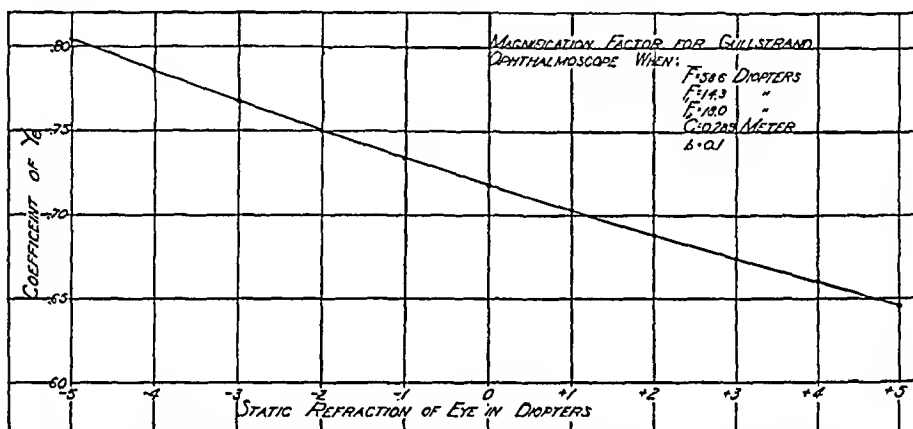
Fig. 3.—Magnification coefficient for the Gullstrand ophthalmoscope.

Since the focal distance of the condensing lens is a function of the optical properties of the ophthalmoscope, and these are kept constant, then this distance is equally constant.

Since the individual refractive error is now the only variable, in order to simplify the use of the formula a curve was charted (fig. 3)

24. We have disregarded that small percentage of cases in which the refracting power of the eye may be altered by distortions of the cornea or other elements of the optical system. In Helmholtz' treatise on physiologic optics it is stated: "The refracting power of the optical system of the eye is equal to the ratio between the focal point angle and the size of the retinal image; but it is not practicable to compare the size of retinal images in 2 different eyes unless the refracting power has the same value for both eyes. For most eyes this seems to be approximately the case." (Helmholtz, H. L. F.: Helmholtz's Treatise on Physiological Optics, translated from the third German edition, edited by J. P. C. Southall, Ithaca, N. Y., The Optical Society of America, 1924, vol. 1, p. 366).

Work is at present in progress to verify the degree of constancy of the refracting power of the eye.

of the magnification coefficient for refractive errors from — 5 diopters to + 5 diopters. Each eye is refracted during the same period of ophthalmoplegia that the measurements are made, the proper coefficient for the particular refractive error is derived from the graph and applied to the measurements and thus measurements accurate to 0.01 mm. are possible on vessels and nerve head in a short time. For example, if a retinal artery measures 0.16 mm. in an eye with a refractive error of + 2.5 diopters, from the graph (fig. 3) one learns that the magnification coefficient of the ophthalmoscope with an eye of + 2.5 diopters is 0.682.

$0.16 \times 0.682 = 0.11$ mm., the true diameter of the artery.

For larger measurements, such as the diameter of the optic disk, it is necessary to take into account the astigmatic error. This was not found necessary for the smaller measurements of the vessels. The horizontal diameter of the optic disk is the measurement usually taken. To correct for measurements taken in this axis, the following formula is used:

$$\bar{A}_H = P + [Q \times cosine^2 (\phi - 90°)].$$

in which the total refraction of the eye is expressed as

P sphere $\subset$ Q cylinder at axis ϕ.

For example, if the diameter of the disk is measured as 1.83 in an eye with a refractive error of — 2.0 sphere $\subset$ — 1.5 cylinder, axis 160, then the error in the horizontal meridian is:

$$\bar{A}_H = -2 + [-1.5 \times cos.^2 (160° - 90°)].$$

The cosine of 70° = 0.342.
$(0.342)^2 = 0.117.$
$-1.5 \times 0.117 = 0.18.$
$A_H = -2 - 0.18 = -2.18.$

The proper coefficient of a refractive error of — 2.18 (from fig. 3) is 0.757.

Then the accurate horizontal diameter of the disk is:

$1.83 \times 0.757 = 1.38$ mm., true diameter of the disk.

The measurements made with this method have proved reliable to 0.01 mm. after repeated determination by different observers. The time required for such determinations is that necessary for complete refraction of the eye plus the few minutes necessary for measurement and calculation. The only technical skill required is familiarity with the Gullstrand ophthalmoscope.

SUMMARY

The history of attempts to measure structures of the fundus has been reviewed and the difficulties of all past methods outlined. The necessity of an accurate clinical method is pointed out.

The Lobeck eyepiece for the Gullstrand ophthalmoscope is described, and the method for its use is discussed. Inaccuracies of Lobeck's original method have been pointed out.

A new method, using the measurements made by the Lobeck eyepiece and applying a formula that takes into account the optical properties of the instrument and the refractive error of the individual eye, is presented. Measurements by this method are probably reliable to 0.01 mm.

RETRORETINAL TISSUE FROM THE CHOROID IN KUHNT-JUNIUS DEGENERATION OF THE MACULA

ANATOMIC STUDY

E. V. L. BROWN, M.D.

CHICAGO

Some of the connective tissue and hemorrhage found in Kuhnt-Junius disciform degeneration of the macula has recently been shown to come from the choroid through breaks in Bruch's membrane.[1] Furthermore, long stretches of vascularized tissue between the choroid and the retina have been reported anterior to the equator in otherwise normal eyes.[2] Indeed, Wolfrum[3] found tissue between the lamina elastica and the basal membrane in older persons thirty years ago, but his observation has been given scant attention. Further data concerning such tissue would therefore seem highly desirable.

In the case reported here long stretches of vascularized preequatorial tissue were found between Bruch's membrane and the pigment epithelium without demonstrable breaks in the membrane.[4] In addition, there was a large mass of retroretinal tissue and blood in the macular region. Capillaries, connective tissue and blood entered this tissue from the choroid through breaks in Bruch's membrane.

REPORT OF A CASE

Mrs. I. P., aged 74, entered Billings Hospital on March 1, 1937, because of failure of vision, first noted two years before. She had been told that she had

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1. (a) Rintelen, F.: Ztschr. f. Augenh. **92**:306-321, 1937. (b) Verhoeff, F. H., and Grossman, H. P.: Pathogenesis of Disciform Degeneration of the Macula, Arch. Ophth. **18**:561-585 (Oct.) 1937. (c) Braun, R.: Arch. f. Augenh. **110**:535-548, 1937.

2. Reichling, W., and Klemens, F.: Arch. f. Ophth. **137**:515-526, 1937. (Eyes were obtained at autopsy from 18 persons. The eyes of 2 persons aged 23 and 33 had small amounts of the tissue, but none was found in the eyes of 9 other persons under 50. The eyes of all of the 7 persons over 50 had long stretches of vascularized tissue between the pigment epithelium and the lamina vitrea. The writers mention no breaks in the lamina vitrea and were not able to determine the source of the tissue.)

3. Wolfrum, M.: Arch. f. Ophth. **67**:307-359, 1908.

4. To be made the subject of a special report.

cataract. Examination revealed small eyes, normal chambers, pupils measuring 2 mm., diffuse granular and vacuolar opacities in each lens and anomalous vessel arrangement on each disk. The right macular region had a large lesion with glistening dots in its lower third. The left macular region was normal, but a large lesion suggestive of extensive chorioretinitis was noted in the fundus below. The tension of the right eye was increased to touch (tension with the Schiötz tonometer was 33 in the right eye and 30.5 in the left eye). Vision in the right eye with correction was limited to perception of fingers at 2 feet (60 cm.); projection of light was normal, and colors and the retinal vascular tree were perceived. Vision in the left eye was 0.8 — 2. A scotoma was found throughout the upper nasal quadrant of the right field, and the central field was reduced to a small area, even for large test objects. The left central field was markedly narrowed. The blood pressure was 152 systolic and 80 diastolic.

A diagnosis of bilateral simple glaucoma, incipient cataract and chorioretinitis, central in the right eye and peripheral in the left eye, was made.

The tension could not be lowered by the use of miotics, so an Elliott trephination with cyclodialysis and peripheral iridectomy was done on March 16 on the right eye and trephination with peripheral iridectomy on the left eye on March 23. Normal tension and vision were secured for the left eye, but a severe iridocyclitis developed in the right eye, and the eye had to be removed three months later because of sudden secondary glaucoma (tension, 71 Schiötz).

Pathologic Report.—Aside from the macular lesion and the trephine opening which was partially closed by newly grown stroma cells, there were edema of the corneal stroma and epithelium, bleb formation, pannus, active exudative and proliferative iridocyclitis, extensive anterior and posterior synechiae, obliteration of the anterior chamber—complete above and almost so below—adhesion of ciliary processes to the iris, forward displacement and swelling of the cataractous lens, rupture of the posterior capsule and an anterior subcapsular cataract corresponding to the position of the sphincter pupillae. The anterior surface of the vitreous showed an albuminous coagulum. There was no glaucomatous cupping of the disk despite weeks of increased tension, and the optic nerve and retina had suffered little change.

Macular Lesion: This lesion proved to be a large mound of tissue lying between the choroid and the retina slightly temporal to the fovea, seated on and merged with a much larger low plateau of tissue of the same type. The latter may be spoken of as a basal lesion tissue.

The basal lesion tissue began at the disk and extended outward 9.54 mm. From above down it measured 8.3 mm.; 4.7 mm. of it lay above and 3.6 mm. below the fovea. Its surface expanse was over twenty-five times that of the disk and eight times that of the mound (fig. 1). Yet the basal lesion tissue did not extend far beyond the mound in any direction except diskward. Normal pigment epithelium and rods and cones were found 2.6 mm. above, 1 mm. temporal to and 3.7 mm. below the mound. Directly behind the fovea the new tissue was 0.09 mm. thick and was nearly 0.1 mm. thick everywhere else in the area between the disk and the mound.

The mound itself (figs. 1 and 2) began 2.12 mm. temporal to the fovea and extended outward 2.62 mm. From above down it measured 3.75 mm., and of this expanse 2.13 mm. lay above and 1.62 mm. below the horizontal meridian. It was 0.58 mm. thick.

Middle-sized and larger choroidal vessels showed marked thickening of their walls behind the mound and to a lesser extent everywhere else, nasal and temporal, posterior to the equator. But there were nearly twice as many vessels whose
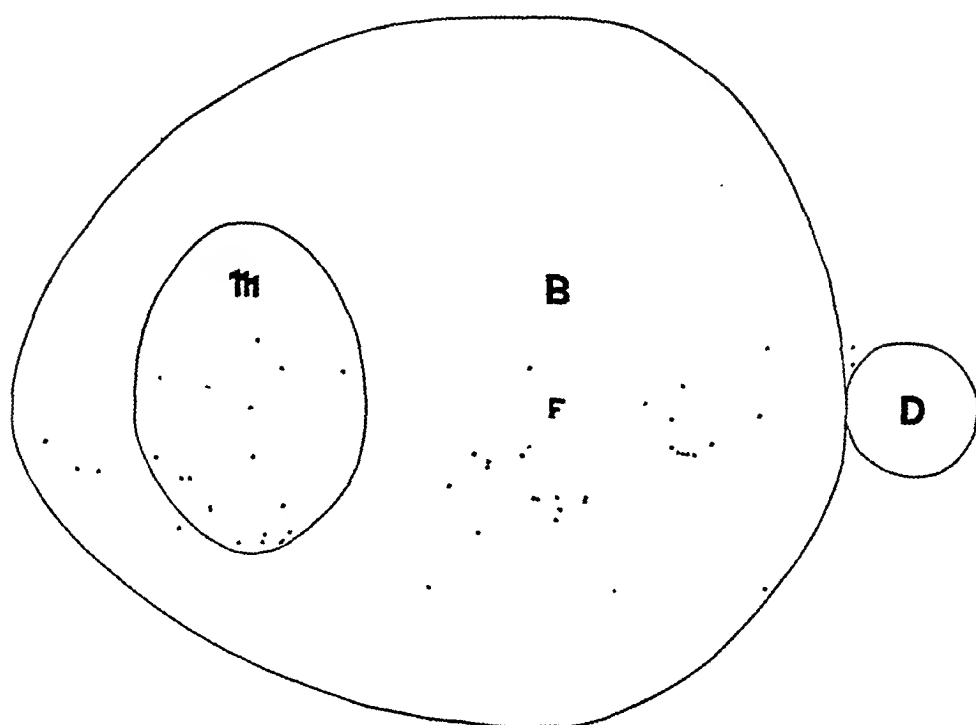
Fig. 1.—Breaks in the lamina vitrea chorioidea. *D* indicates the papilla; *F*, the fovea; *B*, the basal lesion, and *M*, the mound.
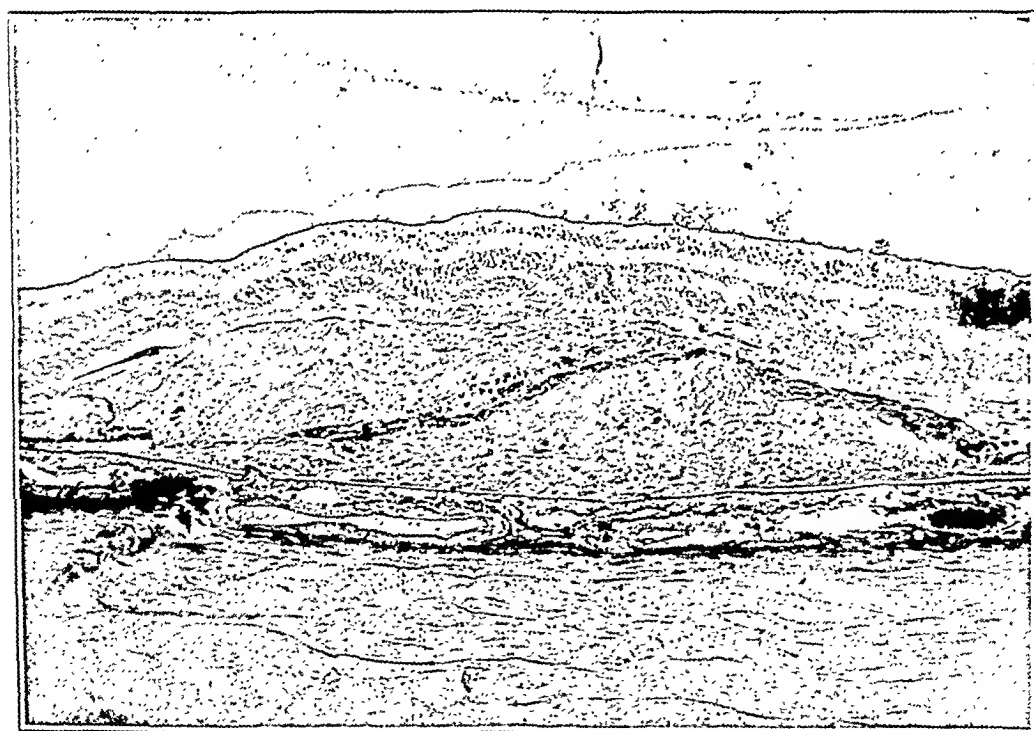
Fig. 2.—The mound. A glial mass is seen in the center next to the retina; × 33.

walls were as wide or wider than their lumens on the temporal side than in a similar area nasal to the disk (75 versus 44 in 11 sections through the level of the disk). A count of thickened posterior ciliary vessel walls in the sclera, episclera and nerve sheath angles on the temporal side as compared with those on the nasal side showed 43 on the temporal side and 24 on the nasal side. On the other hand, the vessels of the optic nerve, papilla and retina showed no thickening of their walls whatever, temporally or nasally, at any level, and the anterior ciliary vessel system was entirely free from thickening of the vessel walls throughout its entire extent.

The rounded surface and sloping sides of the vertical oval mound were conditioned by two or three large masses of tissue partly overriding each other, like oats seeds (fig. 2). One was completely covered and separated from the other by pigment epithelium. All were made up of dense, richly vascularized connective tissue.

The tissue of the mound was directly continuous with that of the basal lesion, and several thin fusiform thickenings of the basal tissue suggested the origin of the mound. Pigmented islands and cells were wholly lacking, and the mass was permeated with old collapsed blood channels. Many of the vessels had thickened walls; indeed, some were definitely sclerosed and many obliterated. Such areas stained less well with eosin; the fibers were closely placed together, were laminated and often changed direction; trains of fibers thus caught in oblique and cross section looked like sclera. The mound was made up almost entirely of this sclera-like tissue. A single or double coat of pigment epithelium covered one mound in an unbroken sheet and lay between it and the other two or three oat-shaped parts of the mass. Good-sized vessels broke through these pigment coats between the portions and carried blood from one to the other. Hyaline degeneration was present here and there, and one series of sections showed cholesterol crystals in a needle-like arrangement, possibly accounting for the glistening dots seen clinically.

Much of the basal lesion was of the same age as that of the mound, but at other levels the tissue was less dense, more vascular and moderately infiltrated with round cells. In some areas each of the four or five lamellas present contained pigment epithelium arranged along the fibers in such a manner as to make it easily possible to hold that the "connective" tissue of the basal lesion was formed from proliferated pigment epithelium (fig. 3). At least half of this "connective" tissue between the disk and the mound was so coated and interlarded with pigment epithelial cells. On the other hand, a large amount of the tissue was closely applied to new and older blood vessels and obviously derived from them. In general, the tissue from the pigment epithelium lay in front of that derived from the vessels; i. e., the pigmented portion lay next to the retina and the vascular layer next to the lamina vitrea. Considerable free blood was encountered in and about the basal lesion tissue, especially above.

The retina was secondarily, not primarily, involved (fig. 2). It was displaced forward slightly by the basal lesion over an area roughly 8 mm. in diameter and still more so by the mound through an area two to three times the size of the disk. Yet the nerve fiber layer, the ganglion cell and the inner plexiform and inner nuclear layers were everywhere intact, continuous and nearly normal. They were free from hemorrhage, fibrin, albuminous coagulum and cell infiltration, and, although there was some spacing apart, there was no other evidence of edema. The outer plexiform and outer nuclear layers, the outer limiting membrane and the rod and cone layer were everywhere destroyed, as such, in front of the mound. A coat of proliferated glia four to eight fibers wide covered the nasal part of the mound and continued over the basal lesion tissue halfway to the fovea.

The retina was firmly anchored to the basal lesion tissue throughout practically the whole extent of the lesion. The exceptions were small areas in which the outer limiting membrane was still intact and a narrow space lay between the retina and the basal lesion tissue. The retina just temporal to, above and below the mound was also fixed to the basal tissue by glial proliferation continuous with trains of cells and fibers from the outer nuclear and outer plexiform layers.

The basal tissue was directly applied to the lamina vitrea choroideae, from the margin of the disk to its outer limits, 9.5 mm. temporal to the disk and everywhere from above downward, 8.3 mm.

Just temporal to the mound the pigment epithelium was found raised into a tiny vesicle 0.03 mm. wide from side to side and 0.005 mm. thick (fig. 4). It extended through 58 sections of 15 microns each and therefore had an expanse
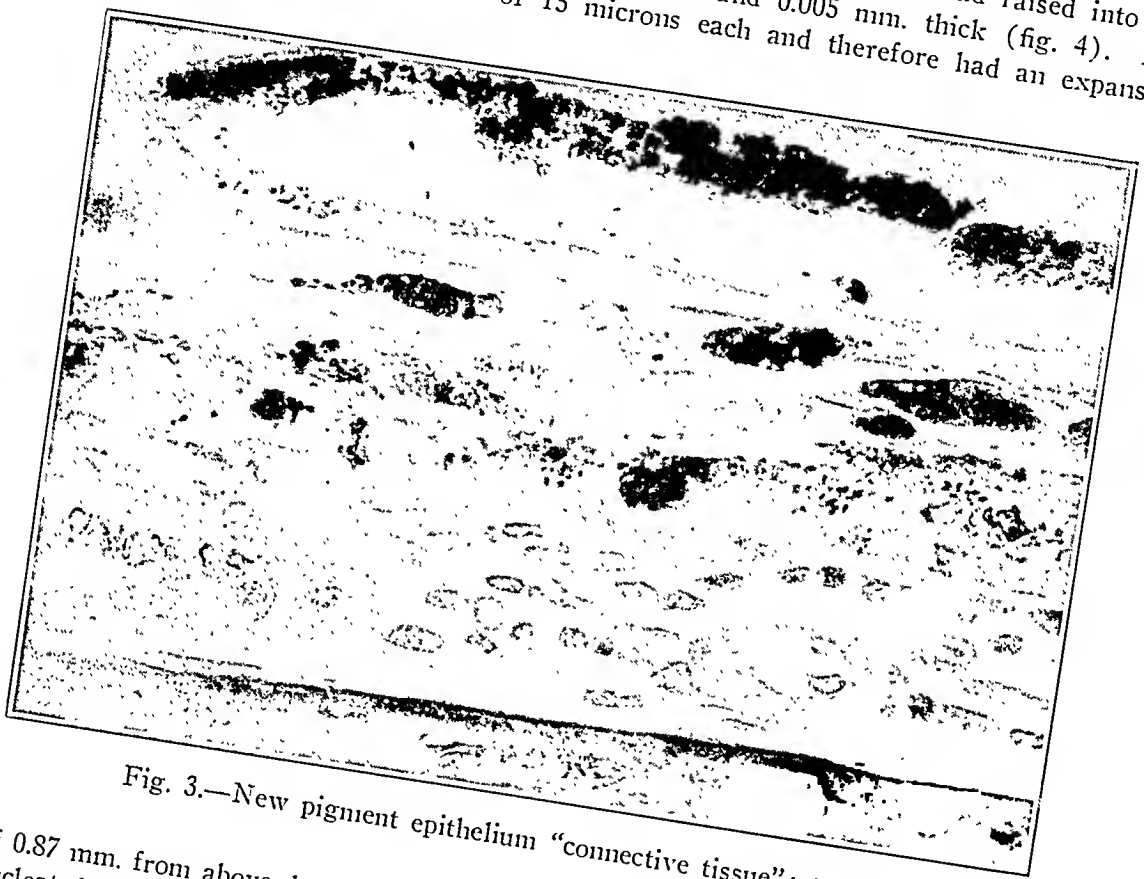
Fig. 3.—New pigment epithelium "connective tissue"; × 750.

of 0.87 mm. from above down. It was filled out almost completely by eccentrically nucleated cuboidal cells with clear protoplasm filled with highly refractile granules. Under high power magnification a few of these granules showed beginning brown pigmentation. No granules were found outside such cells. From their position and makeup it was evident that these cells were newly formed pigment epithelial cells. A break in the lamina vitrea was found at the nasal edge of the vesicle, and the anterior one sixth of the thin wall of a small choroidal vessel half filled with red cells lay in the defect; otherwise the back wall of the vesicle was formed by Bruch's membrane and the anterior wall by the unbroken raised pigment epithelium. Directly in front of the vesicle was a larger space 2 mm. wide and extending through 130 sections, therefore about 2 mm. high from above down. Its posterior half was filled with cells of the same type as found within the vesicle. Several of them had six and eight nuclei. The anterior retinalward half of the space was filled with fibrin. A rod and cone layer was absent, and

some sections showed short breaks in the external limiting membrane, possibly caused by lytic action of the fibrin or phagocytic action of young epithelial cells. One or two of these cells could be seen to have migrated through such a defect and to have attained the external nuclear layer, as in retinitis pigmentosa.

Breaks in the Lamina Vitrea Chorioidea (figs. 1, 2, 4, 5, 6 and 7): Breaks with one or another kind of tissue in or going through them were numerous. Excluding empty breaks, all of which might well have been artefacts, 2 lay near the disk, 32 near the fovea (mostly below it), 13 behind the mound and 4 temporal to it—55 in all (fig. 1). Four breaks below and temporal to the disk were inadvertently omitted. The size of the defects varied from microscopic breaks of 0.007 mm. to 2 of 0.095, 2 of 0.135 and 1 of 0.155 mm., with an average of 0.034 mm. The broken ends of the lamina were sometimes narrowed and indistinct or swollen and were often beveled; one end was frequently bent
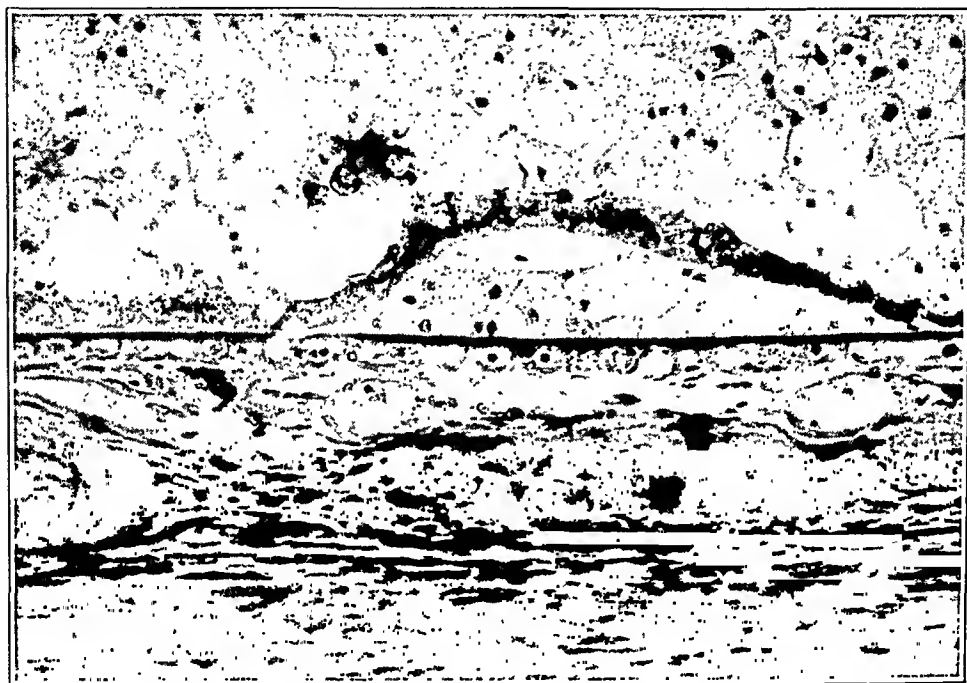
Fig. 4.—Bleb between the lamina vitrea and the pigment epithelium; × 215.

backward at quite an angle; a few had an end buried in new tissue in front of the level of the rest of the membrane. Choroidal tissue was found in 1 break, blood plasma in 3, red cells in 15, pigment epithelial cells in 1, new connective tissue in 12, a capillary or a capillary wall in 6 (figs. 4 and 7) and a larger vessel or parts of its wall in 14 (figs. 5 and 6).

Changes in the Lamina Vitrea and Choriocapillaris: Throughout the area of the lesion one noted an irregular thickening of the lamina vitrea in sections deeply stained with eosin. This irregularity was in constant relation to the adjoining capillary vessels in that the membrane was two to three times as thick between the capillaries as directly in front of them (fig. 6). It often formed the anterior, nasal, temporal and even the posterior wall of these capillaries and shot off obliquely in short or longer spurs or horns for a considerable distance to a point well within the layer of middle-sized vessels. This membrane tissue extension or
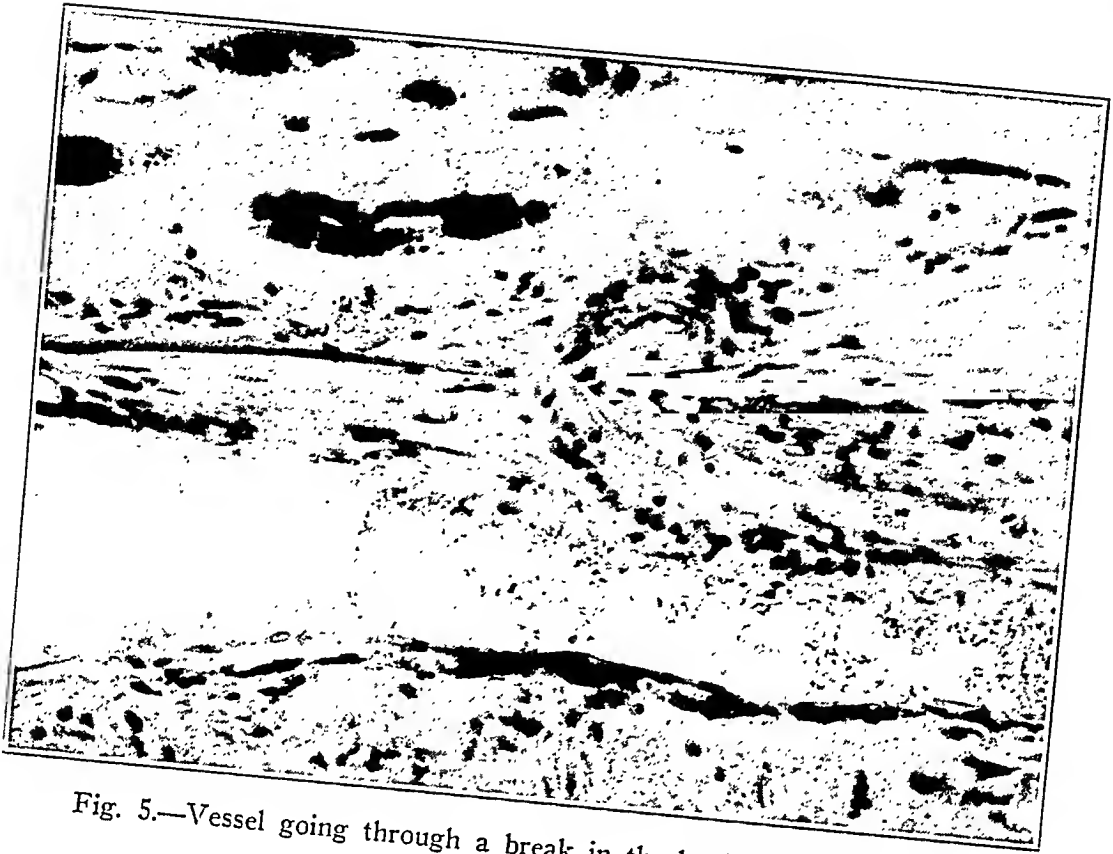
Fig. 5.—Vessel going through a break in the lamina vitrea; × 262.
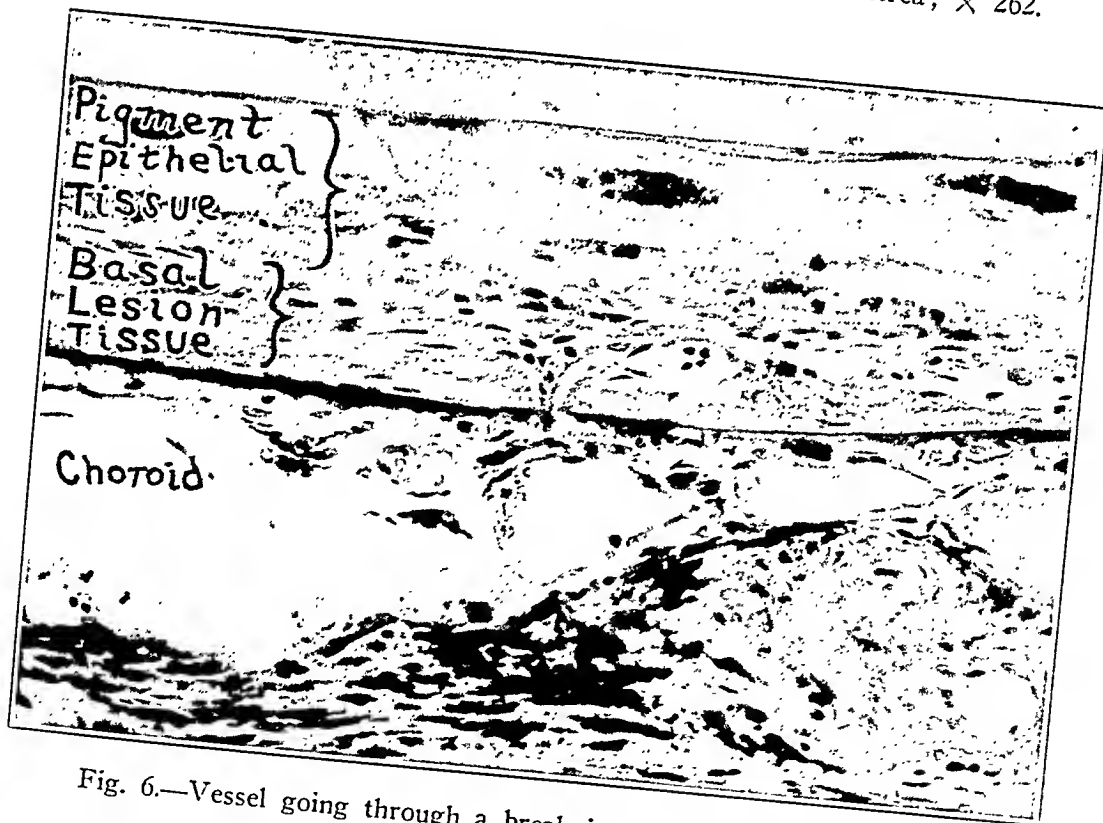
Fig. 6.—Vessel going through a break in the lamina vitrea; × 262.

accentuation was everywhere definitely fibrillated, and the fibrillation extended obliquely across the membrane throughout long stretches, especially well seen near the disk.   No such extension or accentuation of the membrane could be noted temporal to the lesion or on the nasal side of the papilla.   When stained with eosin, it resembled collagenous tissue in every way.   The fibrillation was not of the wavy, crinkly or undulating type characteristic of elastic tissue and conformed to that described and depicted by Wolfrum as extending between the capillaries from the midlayers of the choroid and on to and through the elastic layer of the lamina vitrea, into and across the normally collapsed space between this leaf and the basal (inner) leaf and to the basal leaf itself.[5]   He described his drawings as follows: "Fig. 1: The basal membrane is applied directly to the protoplasm of the pigment epithelium.   On this follows a space filled out by
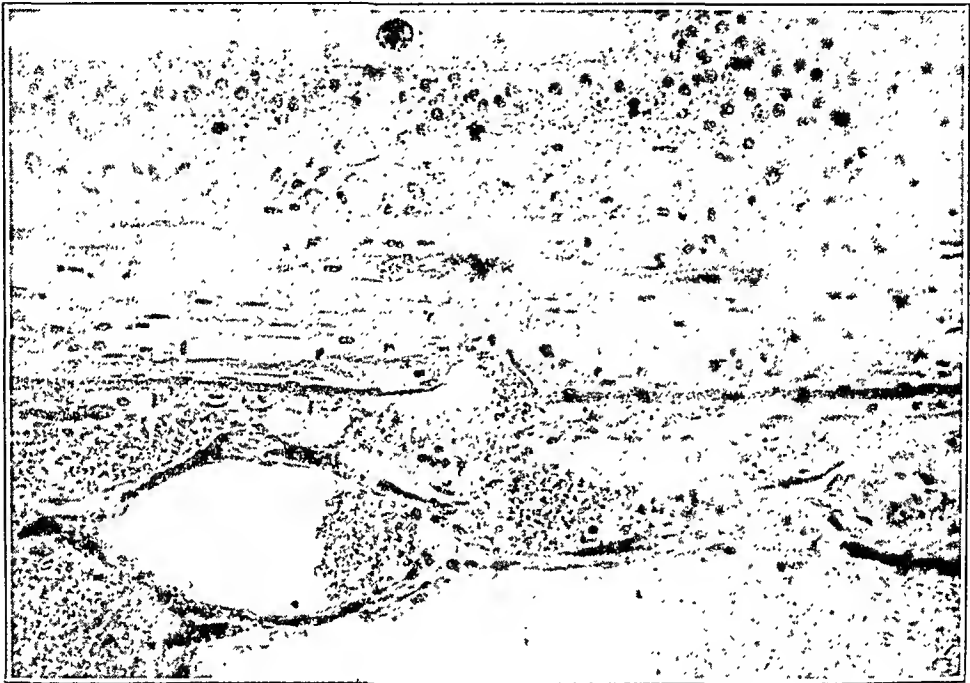
Fig. 7.—Capillary hernia through the lamina vitrea; × 195.

blue stained collagenous fibers (Mallory stain) and on this [posteriorly, E. V. L. B.] follows the lamina elastica (blue red tone; collagen and elastin).   One sees the capillary interstices crossed by collagenous fibers which come out of the choroid and course into the lamina elastica.   Fig. 2 (Weigert stain):   Alongside the dark blue elastic fibers are seen the red collagenous fibers.   The basal membrane is red as is the protoplasm [of the pigment epithelial cells, E. V. L. B.].   No blue fibers go through the cleft between the lamina elastica and the basal membrane."

SUMMARY

A 74 year old woman had a central scotoma accounted for anatomically by a large flat disk of tissue between the macular choroid and the retina and a mound of tissue slightly temporal to the fovea.   This disk

5. Wolfrum,[3] plate XII, figs. 1 and 2.

of tissue was a lesion twenty-five times the size of the papilla and consisted of a broad stratum of proliferating pigment epithelium with a richly vascularized connective tissue layer behind it, i. e., between it and the choroid. The mound consisted of a massing-up of older, previously vessel-rich, unpigmented, sclera-like tissue exclusively of connective tissue type. In front of it lay a defect in the outer layers of the retina. A proliferation of glia fused the retina to the mound. A small vesicle beneath the pigment epithelium just temporal to the mound was filled with proliferating pigment epithelial cells, and a space in front of it contained a much larger mass of the same cells. A defect in the lamina vitrea led into the vesicle. Some 54 other breaks in the lamina vitrea allowed blood, fibroblasts, capillaries and several larger vessels to enter the tissue between the choroid and the retina. Choroidal vessels were badly sclerosed, especially behind the lesion, but vessels throughout the optic nerve, retina and anterior portion of the uvea showed no sclerosis whatever.

PATHOGENESIS

All recent anatomic studies of disciform degeneration show the choroid to be the primary seat of the disease.[6] Retinal involvement, including vascularization, is entirely secondary. It is possible that clinical studies will soon bear this out, for Schmidt[7] has reported that with the binocular ophthalmoscope he could see that the lesion lay behind the pigment epithelium and that the vessels came from the choroid. In my case it is fairly certain that the primary disturbance

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6. Verhoeff and Grossman (1937) and Rintelen (1937) have recently summarized the literature, but several articles have since appeared. I would list the anatomically certain cases as follows: Axenfeld, A.: Arch. f. Ophth. **90**:452-470, 1915. Hegner: Klin. Monatsbl. f. Augenh. **57**:27-48, 1916. Elschnig, A.: ibid. **62**:145-154, 1919. Wölfflin, E.: Arch. f. Ophth. **117**:33-39, 1926. Paul, L.: Ztschr. f. Augenh. **63**:205-222, 1927. Seefelder, R.: Arch. f. Ophth. **120**:139-153, 1928. Behr, C.: Ztschr. f. Augenh. **69**:1-16, 1929. Hanssen, R.: ibid. **72**:360-368, 1930. Behr, C.: ibid. **75**:216-237, 1931. Vogt: Klin. Monatsbl. f. Augenh. **95**:93-94, 1935. Rintelen.[1a] Verhoeff and Grossman.[1b] Terry, T. L., in discussion on Verhoeff, F. H., and Grossman, H. P.: Tr. Am. Ophth. Soc. **35**:262-292, 1937. Braun.[1c] Gifford, S. R., and Cushman, A. B.: Certain Retinopathies Due to Changes in the Lamina Vitrea, Arch. Ophth. **23**:60-76 (Jan.) 1940. Additional anatomically probable cases are those of: Pagenstecher, H., and Genth, C. P.: Atlas der pathologischen Anatomie des Augapfels, Wiesbaden, C. W. Kreidel, 1875; abstracted, Kuhnt, H., and Junius, P.: Die schiebenfoermige Entartung der Netzhautmitte, Berlin, S. Karger, 1926. Michel: Arch. f. Ophth. **24**:131-147, 1878. Hird, R. B.: Tr. Ophth. Soc. U. Kingdom **36**:345-350, 1916. Knapp, A.: Arch. Ophth. **48**:559-562, 1919. Heine: Ztschr. f. Augenh. **60**:1-7, 1926. Reese. A. B., cited by Clay, G. E., and Baird, J. M.: South. M. J. **31**:127, 1938. Possibly the case reported anatomically by H. Friedenwald (Tr. Am. Ophth. Soc. **13**:819-859, 1914) is one of Kuhnt-Junius degeneration.

7. Schmidt, cited by Braun.[1c]

lay in the choroid. Half of the basal lesion and all of the mound was collagenous (connective) tissue (fig. 6). The vesicle just temporal to the mound filled with proliferating pigment epithelium and connected with the choroid through a break in the lamina appears to present an early stage of the process. The larger mass of proliferating pigment epithelial cells in front of it might well represent the second stage. The third would be destruction of rod and cone layer and erosion of the external limiting membrane in tiny bays with migration of pigment epithelial cells into the external nuclear layer, as seen in some of my sections. Transudate and blood from the choroid through numerous breaks in the lamina might well then lift the epithelial mass forward a bit. Glial proliferation over the epithelial mass would complete the picture.

However, this series of events does not explain why breaks in the lamina occur or why retroretinal masses form in cases in which no breaks are to be found despite careful search. In the latter case one needs only to assume that a heightening of the normal flow of fluids from the choriocapillaries through the lamina to the retina has been brought about for some unknown reason, that a stasis of albuminous fluid occurs and that irritation of the highly vital pigment epithelium then results in proliferation. In a 1926 course E. Fuchs ascribed the quiet iritis and secondary cataract of detachment of the retina to a similar process; i. e., albuminous fluid from the choroid accumulates between the pigment epithelium and the retina, passes forward through a tear in the retina, over the pars planum, between the ciliary processes, over the back of the iris, through the pupil, and is absorbed by the anterior surface of the iris into the stroma. In its course forward the iris stroma is the first area which is not protected against the fluid by a double layer of epithelium.

It is not necessary to assume, as does Behr, that there is a primary disease of the lamina vitrea, either of its basal (epithelial) layer or of its elastic tissue layer, though, of course, such a change may actually be the basis of the disease. It is known, for instance, that the elastic tissue in the lamina is the seat of extensive change in angioid streaks in pseudoxanthoma elasticum.[8] Finally, arteriosclerosis has been found in only 4 of the 17 cases previously studied anatomically (Paul, Behr [1931], Rintelen and Braun). Extensive sclerosis of the choroidal vessels was present in my case, was more marked behind the lesion than elsewhere in the choroid and was absent in the retina, optic nerve and anterior portion of the uvea.

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8. Grönblad, E.: "Angioid Streaks"—Pseudoxanthoma Elasticum, Acta ophth. (supp. 1) **10**:1-114, 1932.

CONCLUSIONS

An anatomic study of a case of disciform degeneration of the macula (Kuhnt-Junius disease) in a 74 year old woman is presented. There was considerable opacity of the lens, and clinical data were limited to the observation of a large central chorioretinitic lesion with glistening dots in its lower portion, reduction of vision to counting of fingers at 2 feet, recognition of large objects in a small part of the central field and a loss of the upper nasal field.

A mass of new tissue, 8 by 9 mm. and about 0.1 mm. thick, lay between choroid and retina. Anterior to and continuous with this, and temporal to the fovea, was a mound (or several mounds merged into one). The outer layers of the retina were destroyed in front of the mound and fused to it by glia. The forepart of the basal lesion consisted of pigment epithelium proliferated into a "connective" tissue. The back portion (next to the choroid) was genuine richly vascularized connective tissue, and it continued directly into the tissue of the mound; the latter was old and full of collapsed, obliterated, newly formed vessels but was notably free from pigment. A tiny vesicle lay beneath the raised pigment epithelial layer just temporal to the mound. It was full of proliferating unpigmented pigment epithelium and had a connection with the choroid through a small break in the lamina vitrea near the mound. Other breaks were numerous (54), and through them blood, fibroblasts, capillaries and good-sized vessels made their way from the choroid into the basal tissue and mound. Hemorrhage was abundant on all sides of the mound.

As to pathogenesis, I hold that such definite breaks in the lamina basalis are not really necessary, theoretically, for the formation of such an extensive retroretinal tissue. Changed secretion or simply a marked increase in normal secretion from the choroid and its accumulation into a bleb or vesicle of stagnant albuminous fluid beneath the pigment epithelium would be sufficient to excite marked proliferation of the pigment epithelium. Primary disease of the lamina vitrea could, of course, do this by itself, as held by Behr and others. The large number of breaks found in the lamina vitrea in my case should obviously facilitate both irritation and proliferation of pigment epithelium as well as allow the development of large amounts of connective tissue behind the epithelial tissue. Finally, the process could well have periods of exacerbation and recurrence, as noted clinically.

ADDENDUM: Zandoz'[9] article was received at the library at Billings Hospital on Nov. 24, 1939, a week after this paper was read before the Canadian Ophthalmological Society. It is the first case of bilateral involvement to be so diagnosed and presented clinically before an ophthal-

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9. Zandoz: Arch. f. Ophth. **140**:725-747, 1939.

mologic society as such.   Vogt [10] in 1935 presented the results of an anatomic study of the one eye, and his observations were later confirmed and established by an anatomic study of the second eye by Zandoz, who found many small and numerous larger breaks in the lamina vitrea of each eye (correcting Vogt's statement that the first eye had an intact lamina vitrea) through which capillaries and larger vessels proceeded to a chronic proliferative granulation tissue lens-shaped, tumor-like mass between the choroid and the retina.   A convincing photograph of the fundus and colored drawing of the left eye accompany the text, with illustrations showing the anatomic lesions in each eye.   The author stressed the importance—indeed, the necessity—of serial sections of large expanses of lamina vitrea before one can or should say that no breaks are present. I emphatically endorse this contention.

10. Vogt: Klin. Monatsbl. f. Augenh. **95**:93-94, 1935.

PARADOXIC MONOCULAR PTOSIS

TOMAS R. YANES, M.D.

HABANA, CUBA

An interesting case of paradoxic elevation of the lid, presented by Dr. Sanford R. Gifford,[1] attracted my attention at the same time that I was studying a similar case. A bibliographic research had met with little success, no similar case having been found in the literature. I shall not attempt to give here any pathogenic interpretation of the phenomenon but shall confine myself to the presentation of an illustrative picture, with a consideration of its extraordinary features.

REPORT OF A CASE

A. S., aged 39, in 1932 began to have difficulty with the vision in his left eye, which increased gradually. The condition was not associated with diplopia, vertigo or any other disturbance, nor had the patient had any previous ocular trouble. The disturbance started with a deviation of the eye outward, the upper lid at the same time drooping and occluding the eye almost completely.

The patient was first examined at the beginning of 1938, note being then taken of the existence of incomplete paralysis of the left third nerve, with involvement of the extrinsic muscles and preservation of the pupillary movements. The position of the left eye was that of forced abduction due to the uncontrolled action of the external rectus muscle. Of especial interest was the fact that the ptosis was not absolute but disappeared completely on occlusion of the right eye and when this eye was directed outward or inward.

The media and fundi were normal in both eyes. The vision of the right eye was 20/20; that of the left eye was 1/20, although there was no lesion of the fundus to account for this.

On analyzing the history of the patient, it was found that at the age of 20 he had suffered from a primary syphilitic lesion, which had been insufficiently treated. Six years later, certain manifestations referred to the digestive tract appeared. A diagnosis of gastric ulcer was made, and gastrectomy was performed.

The patient asked for an operation to correct his ocular defect. After explaining to him that functional improvement was impossible and that only an esthetic amelioration was available, on April 30, 1939 I performed recession of the external rectus muscle and tucking of the internal rectus muscle. This brought the cornea almost to a central position. The ptosis improved by about 2 or 3 mm. with the eye in a central position due to the pressure of the lid on the cornea, and

1. Gifford, S. R.: Paradoxic Elevation of the Lid, Arch. Ophth. **22**:252 (Aug.) 1939.

there was slight exophthalmos, which had previously passed unperceived. On August 18 I proceeded to tuck the levator muscle. The condition improved considerably, as may be seen in *A* of the accompanying illustration. The ptosis, of course, still exists.

Although the ptosis is not so marked as it was before the operation, its total disappearance can still be observed, not only when the patient closes his right eye but when the vision of this eye is interfered with by means of a screen or when the patient looks inward or outward with his right eye (*B, C* and *D* of the illustration).

COMMENT

Gifford, in his bibliographic research of this rare phenomenon, found only reference by Bielschowsky to 3 cases reported by Pacetti, in
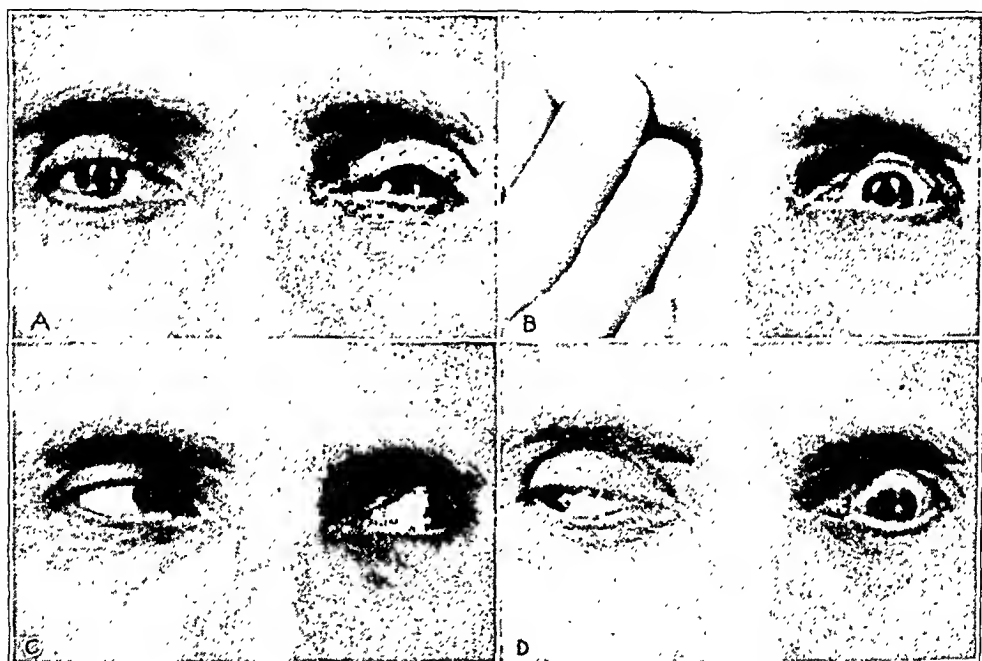
A shows the appearance of the patient's eyes after surgical treatment, which consisted of tucking of the levator muscle, recession of the external rectus muscle and tucking of the internal rectus muscle. Fair results were obtained, but ptosis is still present. *B* shows disappearance of the ptosis when the right eye is closed or screened. *C* shows the absence of ptosis when the patient moves the right eye inward. *D* shows elevation of the upper left lid when the right eye deviates outward.

which each patient presented simple ptosis and the lid opened when the normal eye was closed or screened. However, the original paper has not been consulted, and, consequently, it is impossible to make an accurate comparison.

The resemblances and differences of my case and Dr. Gifford's are tabulated here.

Gifford's Case

Author's Case

1. The condition, observed in the left eye, was acquired.

1. The condition, observed in the left eye, was acquired.

2. There were complete paralysis of the third nerve and paralytic mydriasis of the pupil.

2. There were incomplete paralysis of the third nerve and normal pupillary reactions.

3. There was a history of pneumococcic meningitis with possible supranuclear injury.

3. There was a history of acquired syphilis and probably nuclear lesions.

4. There was paralysis of the vertical movements of the right eye.

4. The right eye was normal in every respect.

5. The anomaly was observed after intervention for ptosis; nevertheless the probability exists that it was present before.

5. The anomaly was observed before any surgical treatment and persisted after it.

6. The ptosis was paralytic due to limitation of the action of the levatoi muscle.

6. The levator muscle of the upper lid retained its full power.

7. During natural winking movements, each time the right lids were closed spastic elevation of the upper left lid was observed.

7. No noticeable movements were observed in the left eye during simple winking.

8. The elevation observed was immediate and was due to the action of the levator muscle, but the lid relaxed afterward. In order to keep the eye opened, the action of the frontalis muscle would be required. The ptosis subsequently persisted.

8. When the right eye was closed, the left levator palpebral vein acted freely and the ptosis disappeared without the assistance of the frontalis muscle.

9. The rapid upward movement of the left upper lid was involuntary and occurred automatically every time the right upper lid was closed, but not when the right eye was screened.

9. The movement also was an involuntary one, but occurred not only during closure of the right eye but even when the vision of this eye was occluded by a screen and when the patient directed his right eye inward or outward.

The possibility of considering the phenomenon as aberrant regeneration of the nerve fibers (a pathogenic hypothesis in the Marcus Gunn syndrome and in the pseudo Graefe or Fuchs's sign), as was done in Gifford's case, is doubtful in my case, in which simple occlusion of the right eye caused retraction of the upper lid without producing any movement in the right eye. One has to accept, therefore, a sensorimotor association.

The closure of the left eye as a defensive movement in order to prevent diplopia was accurately emphasized, but the left upper lid never

could be elevated while the right eye was opened.   Until one is in
possession of a fundamental anatomic basis, any pathogenic interpreta-
tion of this phenomenon would be doubtful and most likely fallacious.
The exposition of my case and the association of it with Gifford's similar
case and possibly with those of Pacetti, form a strong diagnostic basis
which may be used in the study of the complex chapter of the functional
paralysis of ocular movements.

SUBCONJUNCTIVAL LAGRANGE SCLERECTOMY AB EXTERNO

R. J. CURDY, M.D.

KANSAS CITY, MO.

The advantages of the external approach for iridectomy have become well recognized; they are especially evident when a shallow anterior chamber makes the incision by puncture and counterpuncture with the Graefe knife difficult and there is danger of injury to the iris, lens and vitreous. Even more than iridectomy, the Lagrange sclerectomy is difficult and has greater liability to operative accidents. These faults can be eliminated by adoption of the external approach, so that the Lagrange linear fistula can be obtained with no more difficulty and danger than attend the trephine operation.

A long horizontal incision is made in the conjunctiva about 8 mm. above the limbus and undermined to expose the sclera down to the limbus. This is the same as is done for the Elliot trephining operation, except that a longer arc of the limbus is exposed, and the cornea is not split (fig. 1 *A*). An incision is made along the curve of the limbus, about 6 mm. long, perpendicular to the scleral surface and close to the attachment of the conjunctiva at the limbus. A second, more curved incision in the sclera is made above, its middle 1 mm. or a little more from the middle of the first incision and its two ends curving to meet the two ends of the first incision (fig. 1 *B*). This second incision is not perpendicular to the scleral surface but inclined slightly toward the incision at the limbus. The incisions are not made to perforate at first but are sufficiently deep to outline definitely the scleral crescent to be removed. The incisions are deepened slowly by successive light strokes of the knife, and as nearly equally as possible. When perforation occurs, the iris prolapses as it does in trephining, and a peripheral or complete iridectomy can be done without the anterior chamber being entered. Of course, perforation occurs before the scleral crescent is entirely free, but the crescent can be grasped with fine forceps and dissected out easily, preferably after iridectomy. Because of the converging of the scleral incisions, the deep opening of the fistula is a little shorter and narrower than the surface opening; the scleral crescent to be removed tapers to a point at each end and can be dissected out more easily than if the incisions were parallel and with less danger of injury to deeper structures. The iris replaces itself or can be made to do so by slight stroking of the cornea.

The conjunctival flap is replaced and secured in position by such sutures as may be needed (fig. 1 C). A solution of atropine is instilled immediately after the operation and at subsequent dressings if needed. The postoperative care is the same as for the Elliot trephining operation, though there is less tendency to iritis than after trephining. The resulting subconjunctival fistula is long and narrow, with less abrupt sides than those of the fistula made with the circular trephine, with less elevation and thinning of the overlying conjunctiva and probably with less liability to late infection. The internal opening of the fistula is smaller than the surface opening; consequently, the aqueous escapes with diminishing pressure to a large subconjunctival area.
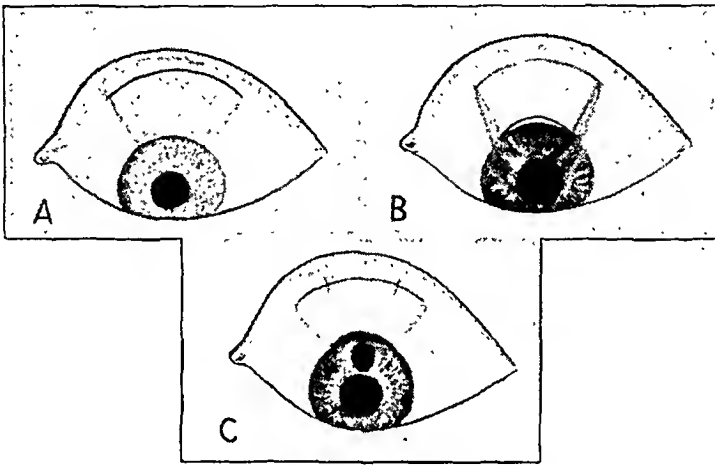
Fig. 1.—Steps of the operative technic.

Fig. 2.—Knife used for the operation.

The scleral incisions can be made with a small scalpel but much better with a special knife made for me by V. Mueller & Co. The blade is 6 mm. long and 2 mm. wide and is placed at an angle of 45 degrees from the line of the shaft, the straight back of the blade making an angle of 135 degrees with the shaft itself; the convex sharp edge is away from the handle and is well bellied (fig. 2). The handle in cross section is octagonal, so that the curved incisions can be made by rotating the handle in the fingers without changing the position of the hand. The length of the blade, 6 mm., is a convenient measure for the length of the incisions and is especially useful when one is operating under the magnification of a loupe.

COMMENTS ON THE TEACHING OF REFRACTION

BENJAMIN FRIEDMAN, M.D.

NEW YORK

The comments presented here are derived from experience gained while teaching refraction to postgraduate students at the Knapp Memorial Eye Hospital during the past seven years. Variations in the procedures of refraction are numerous, each method being acclaimed the best by its particular advocate. A distinct difficulty is to define a standardized routine which will offer the student simplicity in operation combined with maximum efficiency. This difficulty exists despite the fact that procedures of refraction lend themselves with such apparent readiness to an accuracy of assessment not often duplicated in other branches of medicine.

CYCLOPLEGIA AND MYDRIASIS

Not the least important of controversial subjects is the matter of cycloplegia. The following quotation from Verhoeff's[1] review of Cowan's "Refraction of the Eye" illustrates conflicting points of view:

> He [Cowan] makes no definite statement as to when cycloplegics should be used. He implies, however, that they should be used for all patients under 50 years of age. . . . However, in an experience of about forty years, I have found that except in the case of young children cycloplegics are seldom needed. . . .

What is the student to think? His early attempts will readily convince him that cycloplegia is of unquestionable assistance to the beginner in determining the refractive error. But as he progresses in competence he will become less and less dependent on full cycloplegia and full pupillary dilatation. The electric retinoscope bearing an unsilvered reflector is of great value in the examination of small pupils. Armed with fairly accurate retinoscopic findings and after properly fogging the patient's vision, the examiner should not have too much difficulty in arriving at a reliable estimate of the refractive error, even in the undilated eye. Verhoeff's point of view is understandable, therefore, but it presupposes considerable skill, rapidity and consistency on the part of the examiner and at least a measure of intelligence and cooperation on the part of the subject. All this imposes too great a strain on the props of infallibility. I daresay that if an ophthalmologist could review

his failures in refraction he would find that most of them occurred at a time when, for one reason or another, he had decided to conduct the examination without the use of a cycloplegic. It is with an altogether different feeling that he can face the dissatisfied patient if the refraction has been done under cycloplegia; more often than not a neurosis or a general disturbance is the explanation for apparent failure in such cases. It seems illogical, therefore, not to avail oneself of the patent advantages of a cycloplegic, especially with new patients.

The disadvantages of cycloplegia are loss of time to the patient and the physician and the danger of inducing glaucoma in susceptible persons. I hold the time factor to be outweighed by the interests of accuracy. The danger of provoking glaucoma is worthy of more serious consideration. An unrecognized glaucomatous tendency is precipitated into an acute attack by homatropine about once in 10,000 cases. Presumably there must be an occasional case not included because of failure of the patient to return to the refractionist. Because of several unhappy incidents I have made it a rule to employ a weaker cycloplegic in doubtful cases and for nearly all persons over 40 years of age. This leads up to the question of which cycloplegics to employ.

In regard to young children, there is no room for disagreement. For young adults I employ a 2 per cent solution of homatropine hydrobromide. In private practice I use considerably fewer instillations than the accepted average; 1 drop is generally sufficient, and I rarely require more than 2. At the Knapp Memorial Eye Hospital the standing orders call for 4 drops; however, I do not feel that the added drops necessarily induce added accuracy. For patients over 40 years of age, I use ephedrine hydrochloride in aqueous solutions of 3 or 5 per cent. A second instillation is frequently required after fifteen minutes. Ephedrine works poorly in Negroes. The cycloplegia from ephedrine is not marked, as might be supposed, but for the great majority of presbyopes it is a safe and eminently satisfactory drug when proper fogging of the patient's vision is observed. Its virtue lies chiefly in its mydriatic power. If mydriasis is sufficient, I am not too fearful of being tricked by the accommodation. Extreme depression of accommodation is not required for presbyopes. The pupil is readily contracted by a myotic after the use of ephedrine. I find ephedrine more effective than benzedrine. Recent experiences with paredrine,[2] however, lead me to believe the latter to be even more desirable than ephedrine for most presbyopes.

The use of benzedrine and paredrine in conjunction with a 5 per cent solution of homatropine hydrobromide impresses me as a redundancy. So formidable a cycloplegic as a 5 per cent solution of homatropine

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2. Paredrine is a proprietary name for a sympathomimetic drug (4-hydroxy-α-phenyl-β-aminopropane; β-4-hydroxylphenylisopropylamine).

hydrobromide has little need for the weak support of other drugs. What a divergence of opinion between those who do not use any drops and those who recommend a 5 per cent solution of homatropine hydrobromide reenforced by a synergist! Nor do I find that the auxiliary use of benzedrine or paredrine materially speeds the recovery of the eye from cycloplegia. Statements that these drugs do not produce elevation of tension in normal eyes should not be given more value than they deserve. Atropine will not induce glaucoma in a normal eye, but certainly one does not insinuate that it is harmless on that basis. Any drug which causes pupillary dilatation is dangerous to use in an eye predisposed to glaucoma in proportion to its power as a mydriatic.

THE OPHTHALMOMETER

The ophthalmometer does not occupy the position in the refractionist's armamentarium which it once held. At a time when retinoscopy was still undeveloped, the ophthalmometer was a tremendous step forward in the determination of astigmatic errors, but today it is reduced, in my judgment, to little more than a brilliant academic achievement. I have found it to be notoriously inaccurate in the estimation of the strength of weak cylinders and indecisive in the determination of axes of weak cylinders. It is for the low degrees of astigmatic error that one expects performance; the strength and axes of strong cylinders are easy enough to determine without the ophthalmometer. Although there can be no reasonable objection to its use as long as its deficiencies are borne in mind, I personally reserve this instrument for the occasional case in which corroborative information may be required.

ASTIGMATIC CHARTS

Neither am I enthusiastic about the use of astigmatic charts. I prefer to place reliance on retinoscopic examination and on the actual improvement in visual acuity in determining the cylinder. I find the general use of astigmatic charts to consume time and energy disproportionate to the results. Too frequently the patient is uncertain in his responses. This cannot be countenanced, particularly in clinics in which large numbers of refractions have to be done and in which students are in difficulty most of the time, even with the simplest procedures. I believe the Lancaster-Regan charts to be the most desirable. A modified chart of this kind in use with a projection apparatus in which the rotation of the cross is controlled from the examiner's seat is instrumental in saving many steps across the examining room. Undoubtedly astigmatic charts are conducive to refined determinations of the cylindric correction when properly handled, but I believe that equally and more consistently accurate results can be obtained without them.

THE JACKSON CROSSED CYLINDER

Interest has been revived in the Jackson crossed cylinder, chiefly through the efforts of Crisp and, more recently, of Lindner abroad. As an instrument for building up the optimum spherocylindric combination by "crossing through," I find it less satisfactory than the use of its component cylinders taken individually from the trial case. In many instances the latter give more delicate changes and thus represent a slightly more sensitive test. The presence of the spherical element in the crossed cylinder is responsible for this, and it complicates the arithmetic computation involved in calculating the new lens, particularly for the beginner.

The adherents of the Jackson crossed cylinder emphasize its value in determining the strength and axes of cylinders. When the cylindric correction before the patient is perfect in strength, it is assumed that the alternate superimposing of the plus and minus elements will each blur the test line equally. I do not find this to be as reliable an end point as the actual maximum improvement in visual acuity. One ordinarily checks this end stage with a weak plus and minus cylinder from the trial case, thus simulating a crossed cylinder. Crisp has already pointed out that the results with the crossed cylinder are often misleading when the cylinder axis is at 90 or 180 degrees unless the test is carried out with an astigmatic cross.

The Jackson crossed cylinder test for determining axis is based on the following principle: When a cylinder at any axis is crossed by another cylinder of like sign at an angle of 45 degrees a new cylinder is formed the power of which is greater than the power of the separate cylinders and the axis of which lies somewhere between the axes of the individual cylinders. In addition, a weak sphere is formed, but this may be ignored. In practice, the Jackson crossed cylinder is held exactly at 45 degrees to the side of the cylinder in the trial frame and is then rotated to 45 degrees on the other side. If one position is less blurred than the other, the cylinder in the trial frame is displaced slightly in the direction of the clearer angle, and the process is repeated. When the crossings give equal blurring of the test letters, it is assumed that the axis is correct.

I find that the simple procedure of temporarily overcorrecting the cylinder in the trial frame by 0.5 to 1.00 D. and then rotating it a few degrees to either side of the tentative axis is far less complicated and optically accomplishes exactly what the Jackson crossed cylinder does. Much maneuvering and considerable time are thereby saved.

From the foregoing statements, it should be clear that results similar to those obtained with the crossed cylinder may be secured by using the equivalent cylinders individually from the trial case. At any rate, the choice of either method is not an overwhelming one.

MANIFEST AND POSTCYCLOPLEGIC EXAMINATION

I quote further from the review by Verhoeff: "He [Cowan] implies that . . . each patient should be examined three times before the prescription is given." Verhoeff, on the other hand, is of the opinion that "usually a satisfactory prescription for glasses can be given after one examination."

My own experience has led me to adopt a middle course. I dispense with the manifest examination and rely chiefly on the postcycloplegic findings. I believe that the manifest examination is a waste of time and effort when one intends ultimately to use eye drops. A thorough examination of the fundus through the dilated pupil is in itself sufficient justification for the use of a mydriatic. The postcycloplegic examination is the equivalent of the manifest refraction, but it can be done with much greater confidence and celerity because it is based on accurate static findings. Manifest examination, on the other hand, is a more or less exploratory procedure, subject to variations in accommodation and to the inaccuracies of paracentral retinoscopy.

CYCLODAMIA

By this method the vision of both eyes is fogged (without cycloplegia) with the full retinoscopic findings, and the patient is asked to read the Snellen chart. An overcorrection of + 1.50 D. sphere should reduce the vision to 20/200 in each eye. The overcorrection is now lessened by 1.00 D., and the + .50 D. excessive power which remains should blur the vision to 20/40. Reductions are made from these findings for the final prescription.

This method falls short of being sufficiently accurate for popular adoption, but it has two features which are commendable—speed of operation and bilaterality of testing. These factors should be kept in mind while testing by the orthodox methods.

Rapidity should not trespass on accuracy, but the student should understand the fatiguing effect of prolonged examination on both the patient and the oculist. The actual refraction by any method should not consume more than fifteen minutes.

In determining the spherical acceptance at the postcycloplegic examination, the student should be taught to work on both eyes simultaneously whenever practicable. In this manner the patient will accept a maximum of plus and minimum of minus sphere for his optimum vision.

THE RED GREEN TEST

The red-green test is based on the separate refractive values of red and green rays. When it is employed with the accommodation in a

state of relaxation, it is a very sensitive test for the ultimate quarter of a diopter of spherical correction, but in most instances this is hardly necessary.

There is always a danger of permitting a succession of special tests to replace the older and simpler methods as a means of developing clinical judgment. I feel that a multiplicity of refinements in refraction procedure tend to obscure the conception of the problem of refraction as a whole in the mind of the beginner. Painstaking exactness must be encouraged, but one should at the same time combat the notion that minute changes in lens power are invariably essential in writing the final prescription. Above all, the student should be made to realize that the lens which he has so meticulously determined is not necessarily the lens which will offer the greatest comfort. Once having learned the importance of reducing the findings with the trial case, he is less likely to overemphasize the ultra refinements in refraction technic.

CYLINDER RETINOSCOPY, STREAK RETINOSCOPY AND VELONOSCOPY

Cylinder retinoscopy and the streak retinoscopy as methods for the determination of the cylinder axis are not adapted to the limited abilities of the beginner. They make retinoscopic examination more difficult. Refinements in determining the cylinder axis are more easily secured at the trial case. Velonoscopy as an exact check for the strength of a cylinder is not suitable for the average clinical patient because of the time it consumes and the cooperation it requires.

Throughout the field of refraction important methods of examination are preferred by some and rejected by others, yet it is possible for all the dissidents to perform good work. One cannot be arbitrary, therefore, in singling out one procedure as a sine qua non to the exclusion of all others. A particular procedure may yield excellent results to the expert and still be unsuitable to the novice.

CURRICULUM

As a last word, I should like to make some comment on the curriculum of instruction. Short courses are inadequate. The course should extend at least four months, with daily clinical attendance and should include a minimum of 250 cases in which refractive errors are prescribed for by the student under supervision. Enrolment in a course in refraction should be limited to those sincerely desiring to continue instruction in the other branches of ophthalmology and should be contingent on the assurance that the student will pursue such studies. An isolated course in refraction should not be offered.

SHORTENING OF THE EYEBALL FOR RETINAL DETACHMENT

W. E. BORLEY, M.D.

SAN FRANCISCO

The numerous surgical procedures employed for the relief of retinal detachment tend to confirm the belief that the treatment of this condition is still in the empiric stage. With few exceptions, the common surgical operations employed today in treating retinal detachment have as their aim the production of an adhesive choroiditis and the drainage of sub-retinal fluid. Through the pioneering work of Gonin, the necessity of closing the retinal tear when it is present is now well known, the production of the choroiditis being considered essential to bring this about. The separated retina and the retinal tear, however, are the end result of etiologic factors which at the present time appear to be variable and not clearly understood. Although retinal detachments seem to fall into several fairly well defined groups, there are many exceptions and variations. It will not be the purpose here to go into the arguments for and against the various theories as to the cause of retinal detachment, but it will suffice to mention these theories and indicate that there is still no general agreement concerning them.

The theory of traction of the detached vitreous propounded by Leber and Gonin and later amplified by Lindner has a great deal in its favor. On the other hand, Vogt's theory of cystic degeneration of the retina undoubtedly explains a large number of retinal detachments in older persons without myopia. The theory of stretching of the retina in myopia, credited to Hanssen in 1919, does seem a plausible explanation for those detachments falling in the group due to high myopia. Detachments caused by retinal cysts, as described by Weve, certainly form a small but definite group. There is still a fairly large group of detachments without laceration. Although continued observation in cases of detachment of this type may in some instances reveal small peripherally placed holes, it is generally believed that there are a number of detachments which are not associated with retinal tears. Another group of detachments are characterized by their occurrence in young persons, their occasional bilaterality and the presence of oral disinsertions or lacera-

tions not necessarily accompanied by trauma of any severity. Congenital weakness seems to be a factor in the production of these detachments.

The operation of shortening of the eyeball or resection of the sclera was conceived on the assumption that it would relieve the retinal detachment thought to be due to stretching of the coats of the eyeball in cases in which the sclera was elongated. It may not necessarily be limited to this type of case, however, as will be brought out later. Müller [1] appears to be the first to have made use of scleral resection in the treatment of detachment of the retina. It was his theory that retinal detachment in cases of myopia is the result of transudation from the choroid due to the stretching of this vascular layer. The retina is thus displaced by the fluid between it and the choroid. He expressed the belief that if the sclera were shortened the choroid would relax and the cause of the transudation would be removed, allowing the retina to return to its original position. At the time he described his operation, however, the importance of the retinal tear was not realized, so no attempt was made to close it. The successes obtained by Müller in a few instances were probably the result of the inclusion of the retinal tear in an area of choroiditis resulting from the operation. Statistics relative to the location of the retinal tear would bear out this assumption, for it is well known that the most frequent location of the tear is in the superior temporal quadrant, and this, of course, is the area operated on by Müller. In 1903 he reported the case of a man with myopia of 9 diopters in his only useful eye. Retinal detachment developed in this eye, and after medical treatment had failed Müller performed his operation of resecting an oval area of sclera 8 to 10 mm. in width by about 20 mm. in length from the temporal side of the eyeball. The outer wall of the orbit was first resected, Krönlein's method being used. Ten months after the operation the retina was reattached, the field of vision was normal, and the patient could count fingers at 3 meters.

In 1913, before the Vienna Ophthalmological Society, Müller [2] presented 2 cases of retinal detachment in which this method was successful and stated that he had performed the operation on 19 patients. He used the Krönlein procedure to expose the sclera of 14 of these patients. For the last 5, 2 of whom were cured, he exposed the sclera by a widening of the palpebral aperture with temporary division of the superior, inferior and external rectus muscles. He stated that he had used silk sutures and that there was always distinct flattening of the globe subsequently but that the eye was found to have normal tension. In 1 case

1. Müller, L.: Eine neue operative Behandlung der Netzhautabhebung, Klin. Monatsbl. f. Augenh. **41**:459, 1903.

2. Müller, L.: Operative Treatment of Detachment of the Retina, abstracted, Ophth. Rev. **32**:324, 1913.

atrophy of the iris took place. It is interesting to note that he gives as an indication cases in which the detachment has been present for a year as a minimum.

A number of ophthalmic surgeons [3] employed Müller's method with modifications from 1903 to about 1919. The majority of the detachments were due to high grade myopia, and the results were not encouraging, although improvement occurred occasionally. In spite of a fair number of successful results, this operation appears to have fallen into discard, and it was not again revived until 1933, when Lindner [4] reported on a series of 12 eyes operated on by his technic, which is a modification of the Müller operation.

Lindner operated a total of twenty-three times on 12 eyes. With few exceptions the detachments were associated with myopia. Two of the eyes were aphakic with subsequent development of detachment. All the eyes had been operated on previously, with unsuccessful results. Lindner's technic consisted of removing a strip of sclera from 2 to 6 mm. in width and one-quarter to one-half the circumference of the eyeball in length. The scleral incisions were from 8 to 12 mm. from the limbus. Lindner expressed the belief that the best results were obtained after removal of the strip of sclera from the whole circumference of the eyeball, making a two stage operation. In a small number of these eyes there was improvement in the field of vision and a slight increase in visual acuity. In an addendum to Lindner's original article, he stated that the best results are obtained in cases of detachment associated with aphakia, with gross nystagmus and with marked folding of the retina. He also made the statement that it is best to remove only the 2 mm. strips. Any diathermy operation after the shortening may make the condition worse.

Ramach [5] in 1935 published a supplementary report of Lindner's cases relative to changes of the cornea, lid fissure and anterior chamber. He concluded that there was a slight enophthalmos with narrowing of the lid fissure in some cases and a change in the corneal astigmatism in all the cases. In half the cases there was a decrease in depth of the anterior chamber, and in 10 cases slightly decreased corneal sensitivity was present.

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3. Elschnig, A.: Operationslehre, in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1922, vol. 2, p. 1320.

4. Lindner, K.: Heilungsversuche bei prognostisch ungünstigen Fällen von Netzhautabhebung, Ztschr. f. Augenh. **81**:277, 1933.

5. Ramach, F.: Der Einfluss der Bulbusverkürzung nach Lindner auf die Lidspalte, Kammertiefe sowie Krümmung und Empfindlichkeit der Hornhaut, Arch. f. Ophth. **133**:327, 1935.

Lindner has informed me in a recent communication that he is now restricting the use of the shortening operation to cases of aphakia in which the common operations have failed. He expressed the belief that the greatest shrinkage of the vitreous occurs in these cases.

Six cases are reported here, in all of which the prognosis was unfavorable. Previous operations had been performed in all cases, with temporary or no improvement. In 3 of the cases the detachments occurred in myopic eyes. Case 4 is presented with the permission of Dr. Dohrmann Pischel, who operated on the patient. The case has previously been reported in the ARCHIVES.[6]

REPORT OF CASES

CASE 1.—G. S., aged 19, a school boy, on May 18, 1938 was struck in the right eye by a limb of a tree. Vision failed rapidly during the following three days. On examination he was found to have retinal detachment in the right eye. Two operations with diathermy coagulation were unsuccessful. The retina was almost completely detached, and vision was limited to perception of light. In October 1938, while wrestling, the patient noticed poor vision in the left eye, and on examination he was found to have a retinal detachment. An operation on this eye appeared to be partially successful, but on the way home from the hospital the patient suddenly jarred his head and the retina again became detached. He was referred to the ophthalmic clinic of Stanford University School of Medicine for further treatment. Examination on Feb. 11, 1939 showed a completely detached retina in both eyes. Vision in the right eye was limited to perception of light and in the left eye to perception of hand movements at 1 foot (33 cm.) with good projection of light. The retina on the right side was completely detached with degenerated atrophic areas and large strands of vitreous. On the left side the retina was completely detached with a large oral disinsertion at 12 o'clock and a small hole below. Although the prognosis seemed hopeless, it was felt that the patient should be given the benefit of some further surgical procedures. A scleral resection was done on February 18 in the following manner:

After preparation of the left eye, a 1 per cent solution of pontocaine was instilled for surface anesthesia, Van Lint akinesis was done and a retrobulbar injection of procaine hydrochloride and epinephrine hydrochloride was given. The conjunctival incision extended 8 mm. posterior to the limbus from 9 o'clock to 3 o'clock above, or half the circumference of the eyeball. The superior rectus, superior oblique, internal and external rectus muscles were tenotomized, and the sclera was laid bare over the upper half of the globe as far back as 5 mm. past the equator. With a compass and a sharp keratome attachment, the sclera was marked 12 mm. from the limbus and then again 14.5 mm. from the limbus (*A* in the accompanying illustration). By using a small keratome, these incision marks were extended in depth to one-half the thickness of the sclera, and the ends of the parallel incisions were brought together (*B*). Double-arm ooo chromic catgut sutures were then inserted in the edges of the sclera about 1.5 to 2 mm. apart. The strip of sclera was carefully removed without injury to the choroid by the use of sharp dissection with the keratome. An area corresponding in length to three double-armed sutures was removed before application of a 3 per cent solution of sodium hydroxide to the choroid and tying of the first suture. The choroid was

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6. Pischel, D., and Miller, M.: Retinal Detachment Cured by an Eyeball-Shortening Operation: Report of a Case, Arch. Ophth. **22**:974 (Dec.) 1939.

replaced by the use of a spatula. After several sutures were tied, the choroid was found to bulge between the edges of sclera so that it was punctured with a discission knife and the subretinal fluid allowed to drain. This made it possible to continue tying the sutures (C).

There were no postoperative complications and only moderate edema of the conjunctiva and upper lid. Examination of the fundus, however, on March 8 showed the retina to be about as before operation. Vision was limited to perception of hand movements at 1 foot. On March 29 a multiple puncture diathermy operation was performed on the lower half of the eyeball. There was no improvement after this operation.
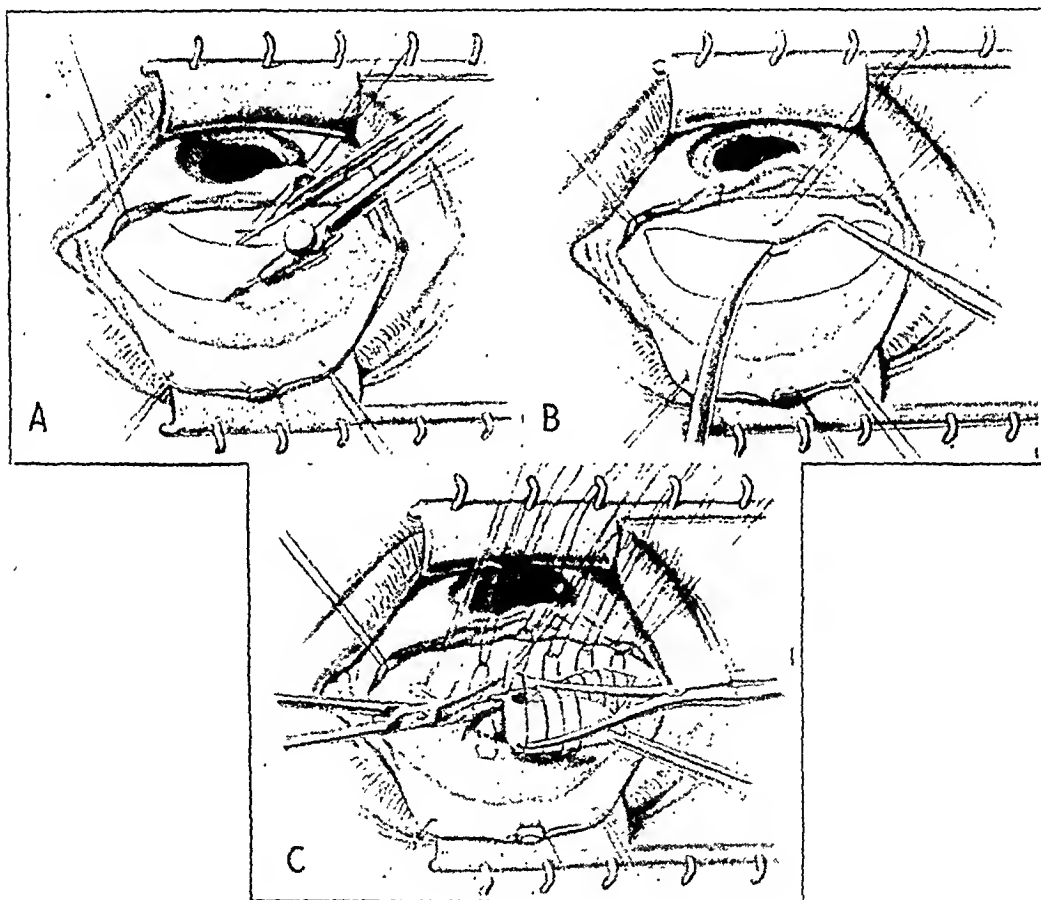
A, technic of marking the sclera. *B*, technic of making the incision in the sclera along the previous marks. *C*, appearance with sutures in place. They are retracted away from the incisions to facilitate removal of the scleral strip. Two sutures are shown tied. (From Lindner.[4])

CASE 2.—R. G., aged 36, a Filipino laborer, had been treated for diabetes and pulmonary tuberculosis at the Clinic of Stanford University School of Medicine for two years. Routine ocular examination on Dec. 15, 1938 revealed detachment of the retina in the lower quadrant of the right eye. Visual acuity was 20/20 in the right eye with a —2.0 D. sphere; visual acuity in the left eye was 20/20. The detachment was bullous in type, and there was a large superior cut in the visual field. The retina appeared atrophic, but no tears were visible. Diathermy surface coagulation was performed on this eye over the sclera below on December 22, with considerable improvement in the field of vision but not complete reattachment. A

flat detachment remained below, which increased in extent during the next six months, until on July 5, 1939 practically the whole upper field of vision was lost. Visual acuity remained good, and no retinal tears were visible. In view of the apparent retraction of the retina below in the presence of extensive choroiditis after the first operation, it was decided to do a shortening operation on the lower half of the eyeball. This operation was done on August 8 at the San Francisco County Hospital. A 2 mm. strip extending from the lower border of the external rcctus muscle to the lower border of the internal rectus muscle was removed. The technic was exactly similar to that described in case 1. There were no post-operative complications. On the last examination, August 2, the retina appeared to be less detached but not completely reattached. There was slight improvement in the field of vision. Myopia had decreased by 1 diopter, but corneal astigmatism had increased. Visual acuity of 20/25 was obtained in the eye that was operated on.

CASE 3.—L. S., a 75 year old school teacher, consulted me first on Oct. 18, 1938, with the complaint of blurred vision of her remaining good .eye for ten days. The vision in the left eye was less than 20/200 because of corneal opacities. Vision in the right eye was 20/200. There was a large bullous detachment in the upper quadrant of the right eye with two large retinal tears. The upper field of vision remained. On October 22 a multiple puncture diathermy operation was done. There was some improvement immediately after operation, but one month later there was still present a flat detachment above, and a few days later the whole lower portion of the retina became detached. Vision was limited to perception of hand movements. On Dec. 10, 1939 a shortening operation was done, a 2.5 mm. strip of sclera being excised from the lower half of the eyeball, 11 mm. from the limbus. The choroid was cauterized with a 3 per cent solution of sodium hydroxide.

After the operation the retina was practically all reattached above for about one month, but it gradually became redetached. There was no improvement below. On the last examination, nine months after the operation, a small area of retina superiorly was in place, and the patient was still able to perceive hand motion in the lower field.

CASE 4.—E. H., a 54 year old housewife, was first examined on Dec. 26, 1937. The left eye had been blind since childhood. The vision in the right eye suddenly became impaired in October 1937. Visual acuity in the right eye was limited to the counting of fingers at 2 feet (60 cm.); visual acuity in the left eye was limited to perception of light. The left eye showed evidence of an old retinal detachment with secondary iritis and cataract. In the right eye the retina was almost totally detached, a small area in the upper nasal quadrant remaining in place. There was a large retinal tear in the horizontal meridian temporally. After a multiple puncture diathermy coagulation operation on December 29 the retina became reattached, and a normal field of vision was present on Jan. 21, 1938. Three weeks later, however, the retina became redetached below with loss of the whole upper field. The original hole was visible, but there seemed to be considerable underlying choroiditis. A second diathermy coagulation operation was performed, pins and surface coagulation being used over the whole temporal half of the sclera. There was no improvement after this operation; the detachment remained the same, and the hole was still visible. The retina appeared slightly atrophic below and had no movement. On June 24 Dr. Dohrmann Pischel did a shortening operation on the whole lower half of the eyeball, removing a 2.5 mm. strip of sclera and coagulating the choroid with a 3 per cent solution of sodium hydroxide.

The only apparent change immediately after operation was a slightly increased motion of the retina below. There was no improvement when the patient was examined two and a half months after operation but on October 13, 1938 or almost

four months after the shortening operation, the retina was found to be completely reattached and the field of vision much improved. Visual acuity was 11/200. On the last examination, Aug. 19, 1939, the retina was found to be still completely reattached, the field of vision was normal and visual acuity was 20/200.

CASE 5.—F. L., a laborer, was first examined in the ophthalmic clinic of Stanford University School of Medicine on July 21, 1938. Vision had been poor all his life, a high myopic correction being necessary. Six weeks previous to his entry the vision of his better eye, the left one, failed. Vision was limited to perception of hand motion at 1 foot in the left eye and was 5/200 in the right eye with correction. Only a portion of the superior quadrant of the field of vision remained. There were several large tears in the retina above. The patient was hospitalized, and a multiple puncture diathermy operation was done on August 3. Three weeks after operation the retina became reattached, and the field of vision was normal. Visual acuity was 15/100 with a —8.0 D. sphere. On examination, September 15, the retina was found to be detached extensively below and on the temporal side. The superior nasal portion of the retina appeared to be in place. A multiple puncture diathermy operation was repeated, an area of sclera from just below the internal rectus muscle to just above the lateral rectus muscle being included. This was done on Feb. 24, 1939. There was no improvement after the operation, and on April 14 an eyeball shortening operation was done over the lower half, a 3 mm. strip of sclera being resected after the same technic described in case 1. On the last examination, Jan. 21, 1939, there was no change in the appearance of the detachment and no improvement in vision, which was limited to perception of hand motions below.

CASE 6.—A 20 year old housewife was first seen at the San Francisco Hospital after an injury to the left eye in 1935. She was kicked in the left eye several weeks before, and on presenting herself for examination was found to have an extensive retinal detachment, with holes below. A diathermy coagulation operation was done below, without success. Approximately two months later a shortening operation was done on the upper half, a 2.5 mm. strip of sclera being excised. There was no improvement in vision, which had been limited to perception of hand movements. Complete records for this case were not available, and the patient disappeared from observation shortly after the second operation.

SUMMARY AND CONCLUSIONS

An operative procedure described by Lindner for shortening of the eyeball by scleral excision is described, with the indications, complications and results in 6 cases.

Cases of myopia with detachment or those in which marked retraction or shrinkage of vitreous is suspected appear to offer the best prognosis after the shortening operation, particularly if no hole is found or if the common operations for detachment which are always done first have not brought about improvement. It is to be noted that Lindner has recently limited the use of the operation to cases of aphakia with detachment.

In 3 of the 6 cases reported, the detachment occurred in myopic persons, in 2 in juvenile patients and in 1 in a senile subject. Two of the three myopic detachments were definitely improved. The others either remained the same or slowly became worse.

CONGENITAL RETINAL FOLD

FREDERICK H. THEODORE, M.D.

AND

JOSEPH ZIPORKES, M.D.

NEW YORK

The observation of 4 cases of congenital retinal folds within six months prompted a study of the subject and is the basis of this report. Apparently no communication on this topic has been published in the American literature, and it was thought worth while to add these cases to those already reported.

REPORT OF CASES

CASE 1.—S. S., a man aged 30, was first seen on Feb. 3, 1939. The vision in the right eye had been poor since birth, and he had always had a lateral nystagmus in each eye. The vision in the right eye was found to be limited to perception of light, unimproved with a + 5.50 sphere. In the left eye the vision was 20/400; it improved to 20/30— with a — 4.50 sphere ⊃ — 1.00 cylinder, axis 118. A marked horizontal nystagmus was present in each eye. Examination of the right eye showed the following positive findings: A broad band of iris arising perpendicularly from the collaret at 6 o'clock formed a persistent pupillary membrane, being adherent to the lens over a broad area ending just below the center. About the adhesion on the anterior lens capsule were scattered V-shaped clumps of brown pigment, of the kind considered congenital. Dilatation of the pupil was incomplete, but as far as could be determined the lens showed no opacities or other abnormalities. The vitreous was normal; no evidence of old inflammation was present.

The fundus showed a most unusual picture (fig. 1). The nerve head was very orange pink and indistinct, due to the fact that it was covered almost entirely by a flat transparent retinal fold. It appeared as if the retina had been pulled over the papilla. Only the nasal quarter of the disk was uncovered, but even here the margin was indistinct. A small clump of pigment was present on the retina over the disk. Immediately above the disk the flat retinal reduplication became accentuated into a sharp gray white fold, elevated several diopters above the remaining retina, as shown by the course of the vessels that went over it. The fold became wider as it coursed anteriorly toward the lens in a superonasal direction. In the region of the ora serrata it divided finger-like into fine strands. Near the disk considerable clumped black pigment was present on the fold. Along almost the entire length of both its margins was more homogeneous pigment. Below the disk the reduplication became a fine fold, which curved gracefully inferonasally, merging into the retina in the equatorial zone. Starting in the mid-

From the Herman Knapp Memorial Eye Hospital.

Read before the Section of Ophthalmology of the New York Academy of Medicine, Nov. 20, 1939.

periphery, somewhat below the main superonasal fold, another fine thin fold coursed parallel to it, similarly dividing into fine strands near the ora serrata. Between these two folds a fairly large depigmented yellow zone was present. Near the disk above and below a number of yellow streaks in the retina associated with pigment were seen. The remainder of the retina showed much fine and slightly coarser pigmentation and was tessellated. A definite macula was not seen. The retinal vascular distribution was more or less normal nasally but temporally was incomplete, arising underneath the folded retina and curving over the folds in a distorted fashion.
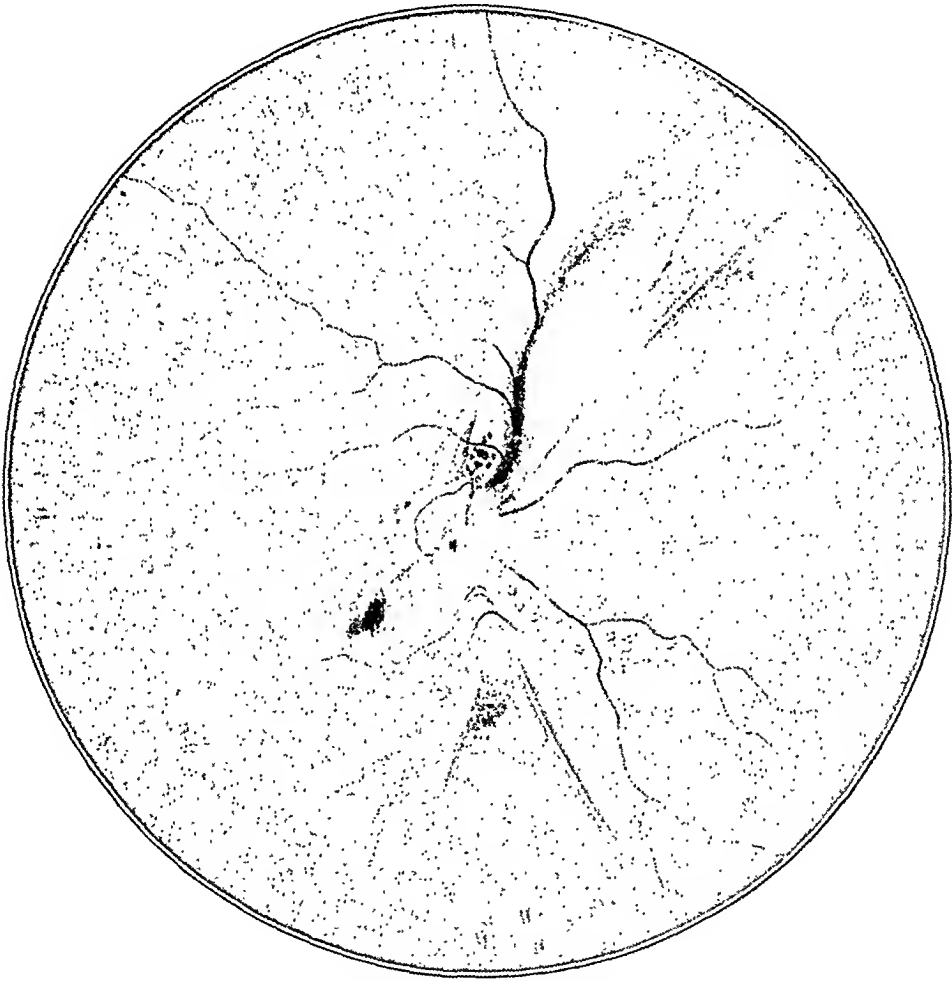
Fig. 1 (case 1).—Drawing of the right fundus.

Examination of the left eye gave negative results except for the fundus. Above the disk there was a thick clump of pigment; 4 disk diameters below was a large area of chorioretinal atrophy with pigment abnormalities. In the extreme periphery temporally a flat gray filmy band involving the internal layers of the retina ran directly perpendicular for a distance of about 4 disk diameters, widening above, to disappear in the adjacent retina. It had no measurable depth.

The patient's father and mother were examined, with negative results. Five brothers and sisters similarly showed no abnormalities. One brother was a twin of the patient, but not an identical twin. One other brother, younger, was found to have bilateral nystagmus since birth. Examination of the fundi revealed some slight depigmentation inferiorly in one eye but gave otherwise negative results.

CASE 2.—J. M., a baby girl 1 year of age, was brought to Dr. Ziporkes' clinic at the Herman Knapp Memorial Eye Hospital in August 1938 because her eyes had been crossed since 3 months of age. Examination was difficult, and general anesthesia was used for the purpose of more complete study, although it was not absolutely required. Perception of light was present, but vision otherwise appeared poor. A right concomitant convergent strabismus was present as well as a bilateral horizontal nystagmus.

Examination of the right fundus (fig. 2) showed the entire nerve head, except for the extreme nasal portion, to be obscured by a broad, gray-white retinal fold
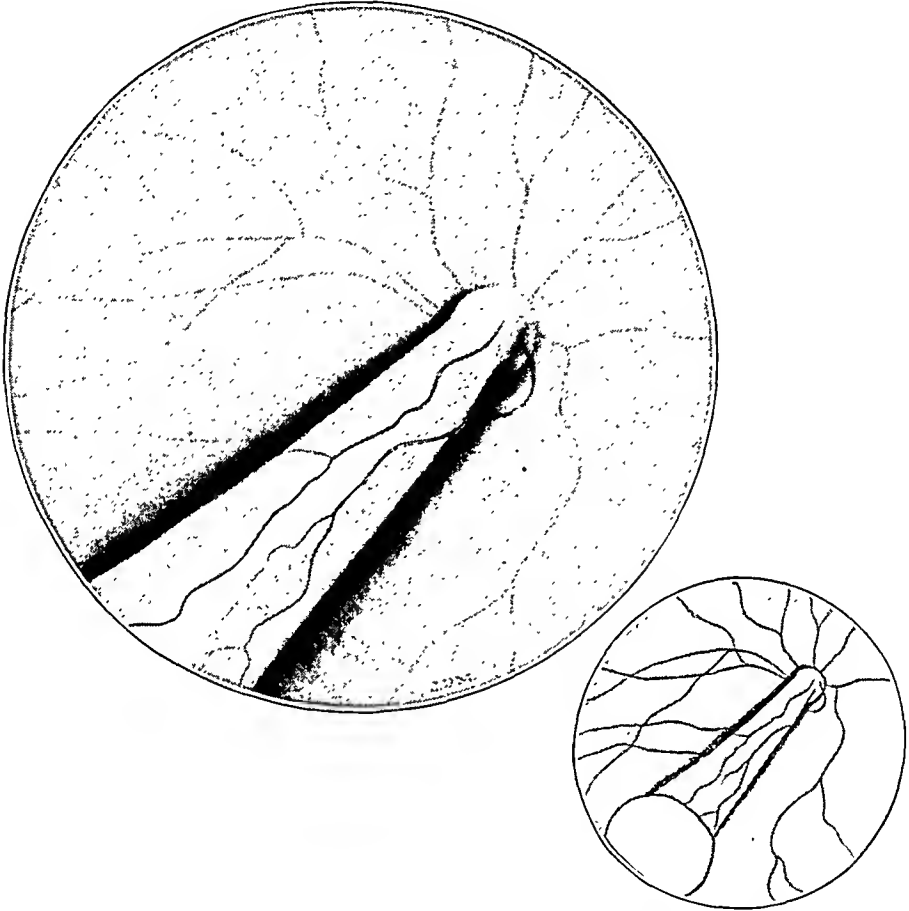
Fig. 2 (case 2).—Drawing of the right fundus. Note the partial cataract in the diagrammatic sketch.

originating from the disk and running inferotemporally to end at the posterior surface of the lens in a circular area occupying the peripheral half of the lower temporal quadrant. The posterior capsular and subcapsular layers were cataractous in this zone. The fold had an elevation of about 2 mm. above the retina and became wider as it went forward, measuring finally 2 disk diameters in width. A heavy continuous line of black pigment demarcated each lateral margin both nasally and temporally. Patent blood vessels could be seen running the entire lengths of the fold. Most arose from the beginning of the fold at the disk; one bent onto the fold from the flat retina. The remainder of the fundus did not

show any abnormalities other than being of the blonde type. The macula was not well seen.

Examination of the left eye (fig. 3) showed an almost exactly symmetric picture. Here the origin of the fold covered the lower half of the optic disk. The disk itself appeared pale. The fold was bordered by pigment only on the nasal side. Lenticular changes exactly similar in character to those in the right eye were present.

The mother of this patient showed notable ocular changes. She had had a congenital cataract of the right eye needled at the Herman Knapp Memorial Eye
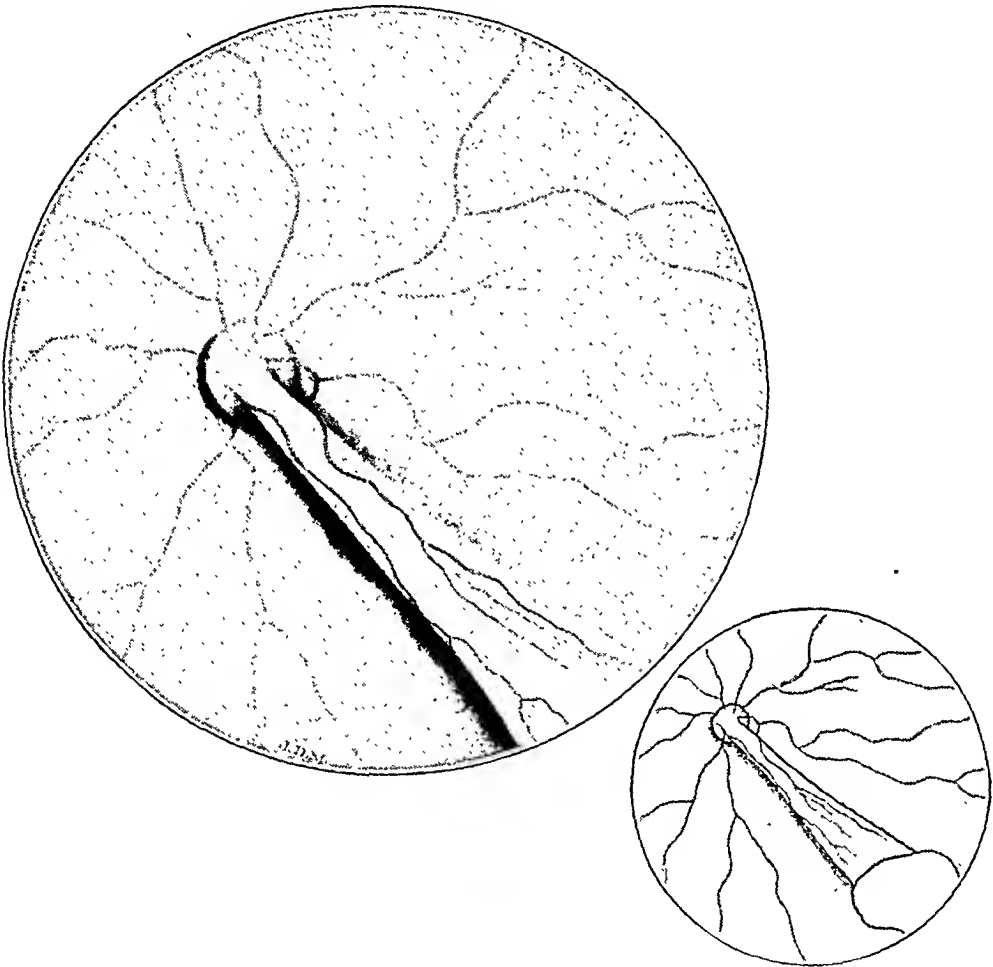
Fig. 3 (case 2).—Drawing of the left fundus. Note the partial cataract in the diagrammatic sketch.

Hospital in 1930. The vision in this eye was limited to perception of light and could not be improved. Interestingly enough, on examination of the fundus a persistent hyaloid artery arising from the temporal portion of the nerve head was found. This was long, running almost horizontally and temporally, to end near the anterior border of the vitreous.

The vision in her left eye could be improved to 20/25. In the lens of this eye fine punctate opacities of the central posterior capsular and subcapsular layers were present. Near the macula were two demarcated areas of old chorio-retinitis, of which at least one appeared to have been fetal in origin.

These findings naturally stimulated study of the entire family. The maternal grandparents of the patient in this case were normal, as were three other children

of theirs and another grandchild. Curiously, four of this group had deep physiologic cups in the left eye only. The father of the patient and his parents were normal.

CASE 3 [1].—S. A., a 44 year old man, had had poor vision in the right eye ever since he could remember. All his life he had strabismus as well. Examination revealed a right hypertropia and exotropia. There was marked weakness of the right inferior rectus muscle and less of the left superior rectus muscle. The vision in the right eye was 20/300, unimproved with a —0.50 sphere. Examination of the fundus showed the presence of a retinal fold arising from the nerve head and running mainly inferiorly and slightly temporally to the region of the ora serrata. The fold was marked temporally by a more or less continuous line of pigment which proximally was clumped. Parallel to it was a fine, straight depigmented line as well. The vasculature of the lower half of the retina was abnormal, apparently due to the fold. Just at the lower margin of the disk two pairs of vessels straddled the fold to supply the retina. Down below at least five vessels emerged through or beneath the fold to supply the inferotemporal portion of the retina and several more emerged to go medially. The remainder of the retina appeared normal, was tessellated and showed scattered drusen. The macula was not well defined but better so than in other cases.

The lens showed no abnormalities.

The left eye was completely normal.

Owing to poor cooperation, examination of the patient's family was limited to one son only. His eyes were normal. None of the patient's children or brothers had poor eyes as far as he knew.

CASE 4 [2].—E. B., a 6 month old baby girl, was brought to the Herman Knapp Memorial Eye Hospital on Aug. 20, 1939, because the mother had noted that the child did not have good vision. Nystagmus was present.

Although the diagnosis of retinal fold was made when the patient was first seen, for completeness of description general anesthesia was used. Perception of light was present, but vision seemed poor. Examination of the right eye showed a marked persistence of the pupillary membrane, characterized by many interlacing strands of varying thickness arising from the collaret. The pupil did not dilate well. The entire posteror cortical and subcapsular layers of the lens were diffusely cataractous, making examination of the vitreous and fundus difficult. All that could be seen was an apparently normal upper portion of the fundus. The region of the nerve head and the entire lower half of the fundus were obscured by a diffuse, gray structure running mainly inferiorly and directly forward into the vitreous toward the lens.

The left eye (fig. 4) showed a similar but less dense pupillary membrane, and the pupil dilated better. The posterior cortical and subcapsular layers of the lens in its extreme temporal fifth were opaque. The nerve head appeared gray and atrophic. Its nasal margin was fairly distinct and edged with a crescent of pigment. Arising one above, the other below, near its temporal borders were two arteries which branched to supply the superior and inferior portions of the retina. The major portion of the disk was covered by tissue confluent with the origin of a broad but relatively flat retinal fold which ran directly

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1. This case was from the service of Dr. J. M. Houlahan.
2. This case also came from the service of Dr. J. M. Houlahan.

temporally toward the periphery. The fold measured about 2 to 3 disk diameters in width and had the appearance of a flat detachment. The central and major portion was gray white and contained two more or less parallel arteries arising just temporal to the disk and running the entire length of the fold. The inferior margin was bordered by considerable pigment. The superior margin was less well demarcated. The remainder of the fundus, except for stippling with pigment, appeared normal.

The patient's mother, father and sister showed no ocular abnormalities. Of the four grandparents, three were normal and the fourth had had good eyesight until bilateral cataracts had supervened, which precluded ophthalmoscopy. In addition, the patient's five aunts and two cousins were normal.
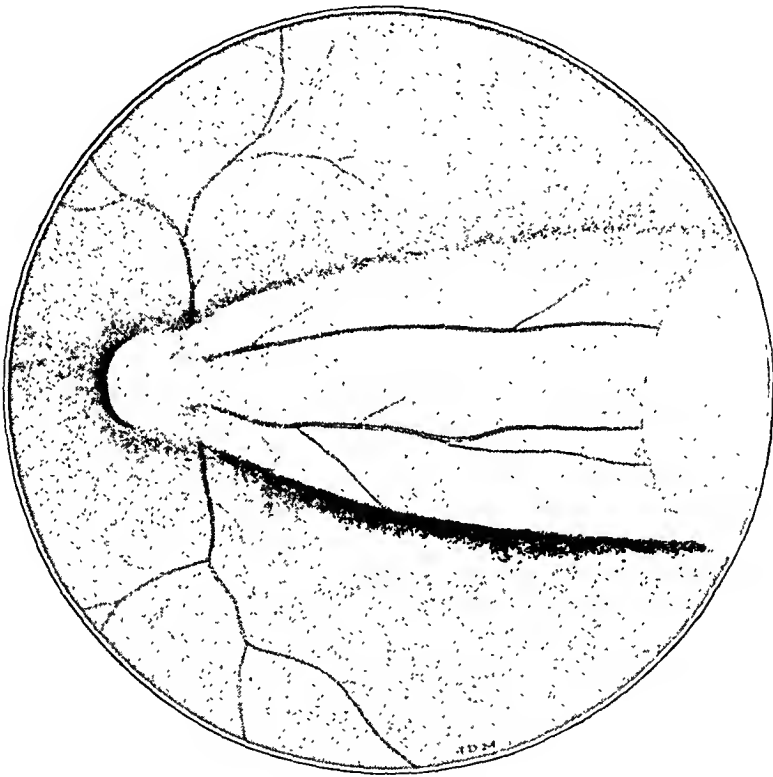
Fig. 4 (case 4).—Drawing of the left fundus. Note the partial cataract.

REVIEW OF THE LITERATURE

While early investigators must have encountered congenital retinal folds and did describe abnormalities similar to them, it seems that the first to recognize the condition as a distinct congenital abnormality was Sulzer,[3] who in 1888 reported the occurrence of such an anomaly in a half Javanese, half European boy. The involvement was unilateral, the fold going inferotemporally. Additional findings included a congenital cataract distinct from the fold and a persistent pupillary membrane.

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3. Sulzer: Gefässhaltige Ueberreste des hinteren Abschnittes der gefässhaltigen fötalen Linsenkapsel beim Erwachsenen an einem Auge mit Membrana pupillaris perseverans und anderen Entwicklungsanomalien, Klin. Monatsbl. f. Augenh. **26**:425, 1888.

·After him, in 1902 Salffner [4] reported the results of a pathologic examination of an eye enucleated for fear of glioma, in which he found a retinal septum arising from the disk and adherent to a persistent hyaloid artery and the back of the lens.   In 1904 Heine [5] reported 2 cases, the anomaly being observed clinically in 1 case and at pathologic examination in another.   He expressed the belief that the condition was essentially cystic and noted maldevelopment of the entire retina.   The next case report was made by de Vries [6] in 1908, who described a rather typical case but considered the anomaly a persistent hyaloid artery covered with connective tissue.   The posterior half of this eye was examined anatomically by Ancona [7] in 1935.   In 1923 the first case of bilateral symmetric involvement of the eyes was reported by Holm.[8]   In 1926 Hoffmann [9] added another case, only one eye being involved.   In 1927 Metzger [10] published a stereophotograph of a retinal fold. Various theories were propounded by these authors, who for the most part were entirely unaware of the contributions of the others.

In 1928 Ida Mann [11] described the results of pathologic examination of a congenital retinal fold and formulated a theory as to its origin.   By 1935 [12] she had seen the condition in 6 cases, a total of 8 eyes, 3 of which had been sectioned pathologically.   In 1937 [13] she again discussed her conclusions about the condition, which will be briefly summarized here. Mann expressed the belief that these anomalies are not colobomas but folds or ridges involving the inner layer of the optic cup and that there is a defect in the gross structure and differentiation of the inner layer of the optic cup, occurring mostly after the 13 mm. embryonic stage.   The pigment layer is uninvolved, but the inner layers are disturbed, distorted and imperfectly differentiated.   Atypical rosette formation is noted as. well as hypoplasia of the retinal layers.   In all the eyes examined microscopically the whole retina, not only the reduplicated, folded portion,.

4. Salffner, O.: Bulbus septatus, Arch. f. Ophth. **54**:552, 1902.

5. Heine, L.: Klinisches und Anatomisches über eine bisher unbekannte Missbildung des Auges: Angeborene Cystenretina, Arch. f. Ophth. **58**:38, 1904.

6. de Vries, W. M.: Arteria Hyaloidea Persistens, Nederl. tijdschr. v. geneesk. **44**:1399, 1908.

7. Ancona, S.: Case of Persistence of Primary Epithelial Optic Papilla (von Szily), Nederl. tijdschr. v. geneesk. **79**:135 (Jan. 12) 1935.

8. Holm, E.: Coloboma corporis vitrei, Acta ophth. **1**:63, 1923.

9. Hoffmann, H.: Ueber eine seltene Strangbildung im Augenhintergrund, Klin. Monatsbl. f. Augenh. **77**:370 (Sept.) 1926.

10. Metzger, E.: Die Stereophotographie des Augenhintergrundes, Klin. Monatsbl. f. Augenh. **78**:338 (March) 1927.

11. Mann, I.: A Case of Congenital Abnormality of the Retina, Tr. Ophth. Soc. U. Kingdom **48**:383, 1928.

12. Mann, I.: Congenital Retinal Fold, Brit. J. Ophth. **19**:641 (Dec.) 1935.

13. Mann, I.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, p. 219.

showed this imperfect differentiation. Furthermore, in all cases in which microscopic examination was done and in many in which the condition was observed clinically she found an attachment of a branch of the hyaloid artery to the apex of the fold. She suggested that the deformity is produced by an abnormal adhesion of the primary vitreous to the inner layer of the optic cup, which does not separate as the secondary vitreous appears and results in a pulling up of the retina in a narrow tentlike detachment. She saw no signs of fetal inflammation, nor did the general hypoplasia of the entire retina make this likely. In most, but not all, of her cases the folds were inferotemporal. This she could not explain.

This excellent work was complemented by the extensive reports of Weve,[14] the first of which appeared in 1935 and the second in 1938. In contradistinction to the essentially anatomic studies of Mann, Weve's investigations were conducted mainly clinically, one pathologic specimen being examined. His findings are important and must be noted. To begin with, Weve saw definite retinal folds in 5 cases, a total of 6 eyes. In 2 of the cases of unilateral involvement the other eye showed what he called a sector-shaped, slight, flat detachment, arising next to the disk and going temporally and containing several long, straight, stretched-out vessels running its entire length. This "detachment" was likewise present in both eyes of the identical twin of one of the aforementioned patients and in one eye of the grandmother of another patient. Moreover, 2 other patients with retinal folds had relatives, in one instance a brother and a second cousin and in the other instance a sister, who were all found to suffer from pseudogliomas. On the basis of these interesting cases, Weve concluded that the curious flat detachments (ablatio pellucida), the definite retinal folds (ablatio falciformis) and the pseudogliomas are all varying degrees of the same congenital abnormality, the first being a sort of "forme fruste" and the last an exaggerated manifestation of a retinal fold. The forme fruste, he pointed out, in itself might easily have been overlooked and considered an anomaly of vascular distribution. He was convinced of the familial if not hereditary character of the condition and found consanguinity in many of the parents of his patients. In this connection he took issue with Tillema,[15] who in 1937, after a pathologic study in which he found evidence of inflammation, suggested that fetal inflammation of the inner layer of the optic cup might cause this condition. Weve frequently

14. Weve, H.: Ueber "Ablatio falciformis congenita," Arch. f. Augenh. **109**: 371 (Dec.) 1935; Ablatio Falciformis Congenita (Retinal Fold), Brit. J. Ophth. **22**:456 (Aug.) 1938.

15. Tillema, A.: Infantile and Congenital Retinal Fold, Brit. J. Ophth. **21**: 94 (Feb.) 1937.

noted other congenital abnormalities, such as persistent pupillary membranes and opacities of the lens, in these cases, but not persistent hyaloid arteries. Except for 1 case, all the folds were in the inferotemporal portion.

In his first paper Weve spent considerable time on the question of the mode of origin. He expressed the belief that there was no significant relation to the persistence of the hyaloid artery and that the tissue involved was proliferative. He thought that adherence of the retina to mesodermal tissue in the anterior half of the eye is the primary abnormality and that the folds occur as a result of traction. He stated that it was not due to the persistence of a portion of the primitive epithelial papilla (Schalstück) of von Szily, as Ancona, after a study of de Vries's case, had stated earlier in 1935 and as Kiewe[16] was to reiterate in 1936.

Only 2 other reports on congenital retinal fold remain to be mentioned. Both appeared in 1936 and were short case reports. Evans'[17] paper contained a clinical description of one of Mann's cases in which the condition was studied pathologically. The other, written by Iles,[18] described a fold going superotemporally, containing remnants of hyaloid tissue.

COMMENT

The cases described at the beginning of this paper conform closely to those described elsewhere and must be considered rather typical cases of congenital retinal fold. They confirm the following observations of previous authors:

1. The folds are often bilateral and, if so, symmetric and usually directed inferotemporally.

2. The folds are usually bordered by a heavy line of pigment, and considerable pigment is scattered over the remainder of the fundus.

3. The retina otherwise is abnormal and the macula poorly developed.

4. The vascular distribution of the retina is abnormal.

5. The lens is cataractous where the fold comes forward.

6. Other congenital abnormalities occur frequently, notably persistent pupillary membrane of marked degree.

7. Nystagmus is present.

16. Kiewe, P.: Beitrag zur Kenntnis der angeborenen Missbildungen des menschlichen Auges: Persistenz des Schaltstücks (v. Szily); Heterotopie der Netzhaut und Canalis hyaloideus persistens, Arch. f. Ophth. **135**:220 (March) 1936.

17. Evans, P. J.: Congenital Fold of Retina, Tr. Ophth. Soc. U. Kingdom **56**:344, 1936.

18. Iles, A. E.: Congenital Retinal Fold, Proc. Roy. Soc. Med. **29**:390 (Feb.) 1936.

8. Vision is markedly impaired.

9. There is a superficial resemblance to retinitis proliferans.

Moreover, in these cases, not previously recorded, the patients would include adults.

Furthermore, in case 1, as Mann noted, it is seen that there can be several folds present in the same eye and that they may originate away from the disk. Besides, these secondary folds are very flimsy and feathery and may represent another type of forme fruste. Indeed, the formation in the good eye of this patient might be of this nature. In case 4 the right eye might be considered almost pseudogliomatous.

The only confirmation of Weve's theory that the condition is hereditary or at least familial was obtained in cases 1 and 2. In case 1 a younger brother had congenital nystagmus. Case 2 is particularly interesting in this connection, since the child's mother had had a congenital cataract and showed a complete persistent hyaloid artery going all the way forward to the lens. Moreover, in the other eye she had suggestive signs of congenital involvement. If Mann's concept that a persistent hyaloid artery is present either clinically or on section in all cases of retinal fold is correct, then this case is even more important from the hereditary aspect. No consanguinity was found in our cases. However, we feel that parents having a child with this condition should be advised as to the possible familial character of the anomaly. The children of the patient in case 3 apparently were normal, but Weve expressed the belief the condition is a recessive characteristic.

Rather than speculate as to the nature of the exact cause of these folds, we would refer the reader to those who have studied anatomic preparations, and we are inclined to accept Mann's explanation as the most likely. Fundamentally, Weve's theory of formation of these folds by adhesion between the retina and the mesoderm of the anterior half of the eye is similar to Mann's concept, since she believes that all of this mesodermal tissue forms part of the primary vitreous. It is perhaps more important to stress the seriousness of the condition and the possibility that more cases may eventually be seen, particularly when children in institutions for the blind are examined with the abnormality in mind.

GLAUCOMA FOLLOWING IRRADIATION

PATHOLOGIC REPORT

LOUIS BOTHMAN, M.D.
CHICAGO

Clinical reports of glaucoma following the use of roentgen and radium therapy are infrequent. In a survey of the ophthalmic literature, only 3 pathologic reports were found.

In 1921 Birch-Hirschfeld[1] reported the case of a 61 year old man who twenty years before had a wart on his right upper lid. This was removed in 1914 but reappeared in 1919 and grew larger. The lid was treated with five exposures to the roentgen rays of forty-five minutes each in the course of one year, without protection to the globe. Two weeks after the first dose the patient had headache, pain in the eye and redness of the skin of the lid and conjunctiva. These symptoms disappeared between exposures but reappeared with each treatment.

When he was examined in May 1920 there was an epithelized scar on the lid, the margin of which was free from cilia. The conjunctiva of the lid was thickened and chemotic and had numerous dilated, tortuous blood vessels. A thin, vascularized pannus lay on the upper part of the cornea near the limbus. The cornea was opaque due to deep and superficial infiltrates. Its surface was dull and smooth. The iris was atrophic, the pupil was of maximum width and the tension with the Schiötz tonometer was 40 mm. of mercury. The eye was blind. The left eye was normal.

Histologic examination revealed perivascular hemorrhage from serous transudates in the conjunctiva. The basal cells of the corneal epithelium were flat and had rod-shaped nuclei. The next layer was poorly stained, and the cells were vacuolated, irregularly shaped and degenerated. The external layer consisted of a row of flat cells. In some places the epithelium existed only as a single layer of cells. The conjunctiva immediately around the cornea contained plasma cells in the subepithelial tissue. There were tortuous blood vessels, some with narrowed and others with wide lumens. The pannus-like tissue

1. Birch-Hirschfeld, A.: Ztschr. f. Augenh. 45:199-206, 1921; Strahlentherapie 12:565-572, 1921.

extended even into the deep layers of the cornea. There was dustlike pigment on the anterior surface of the iris. The iris and ciliary bodies were atrophic and their blood vessels obliterated. The walls of the retinal blood vessels were thin, their endothelium was elevated and their adventitia was thickened. The perivascular spaces were widened, and the perivascular glial fibers were separated and torn. The disk was pathologically cupped, and the nerve fibers were atrophic. There were fine, striated hemorrhages in the retina.

In a case of conjunctival carcinoma reported by Peters [2] glaucoma appeared one year after the last of a series of roentgen treatments. The eye was removed and studied. It revealed sclerosis of the ciliary processes, which appeared short and shrunken. The fibrils of connective tissue were interspersed with thick cells, which had little collagenous tissue and fine nuclei. There were some scarred chalklike dots. There was no sign of inflammation. The blood vessels were not diseased.

In 1904 Birch-Hirschfeld [3] exposed rabbits' eyes to therapeutic doses of roentgen rays and made a pathologic study. He found partial degeneration of the retinal ganglion cells with vacuolation of the protoplasm, dispersion of the chromatin substance and shrinkage of the nuclei and cells. There was degeneration of the nerve fibers and their medullated sheaths.

He reported the case of a 59 year old man who had a malignant condition of the skin of his temple, for which he received six exposures to the roentgen rays of twenty minutes each and one exposure of forty-five minutes' duration during ten months. There was no glaucoma. The tumor extended onto the globe, and the eye was enucleated. The ciliary epithelial cells were poor in protoplasm and in pigment. The walls of the blood vessels of the iris were thick, and the lumens were narrow. The pigment in the stroma was sparse. There was dustlike pigment on the anterior surface of the iris. The pigment on the posterior surface of the iris was vacuolated and swollen, and the dilator muscle was easily seen. There was no pigment in the spaces of Fontana. A thin membrane extended from Descemet's membrane over the pectinate ligament in a portion of the globe. The retinal blood vessels, even the central retinal vessel, had narrowed lumens. There were normal nerve fibers in the optic nerve, with a physiologic excavation. The ganglion cells of the retina were involved; scarcely any were normal. There was loss of chromatin, shrinkage of the nuclei and dissolution.

This last case is mentioned to show that the pigment disturbance followed roentgen therapy to the eye without causing glaucoma. Both of Birch-Hirschfeld's patients, as well as rabbits he used for experi-

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2. Peters, G.: Strahlentherapie **17**:189-191, 1924.
3. Birch-Hirschfeld, A.: Arch. f. Ophth. **59**:229-310, 1904.

mental work, showed similar changes, which he believed arose from injury to the blood vessels from the roentgen rays.

It was my intention to present 3 cases with changes in the eye following irradiation, in all of which parallel alterations occurred. Space will not permit that all be described in detail.

REPORT OF CASES

CASE 1.—A man, aged 60, had a sarcoma of the choroid of the right eye. There was an incipient cataract in the left eye, and the tension was normal. The patient had received irradiation with 600 roentgens. The disk had a glaucomatous excavation. There were rarefaction and dispersion of pigment in the ciliary processes and iris. Sclerosis of the pectinate ligament and pigment in the spaces of Fontana were observed in one third of the sections.

Because the tumor was pigmented and because any intraocular neoplasm can cause glaucoma, this case is not presented in detail.

CASE 2.—A 46 year old woman had received considerable radium therapy but no roentgen treatment for carcinoma of the right limbus. She had a cataract in the right eye but no glaucoma. The left eye was normal. There was no pigment in the pectinate ligament, though the iris pigment was so markedly vacuolated that it appeared honeycombed, and the ciliary pigment epithelium was thinned or absent in many sections.

CASE 3.—*History.*—A man, aged 62, was first seen by me on May 27, 1936, complaining of poor vision in his left eye for six months. He thought the vision before that time had been as good as that in his right eye. The eye felt irritated but had no definite pain.

Examination by Dr. Ernest McEwen in February 1914 revealed a small wart at the external angle of the right eye, which the patient stated had been present for eight months; it was covered by a dry crust surrounded by a mild dermatitis. This was treated by Dr. McEwen,[4] who gave seven roentgen or radium treatments to the lid between February and April 20, 1914. He was apparently free from symptoms until January 1929, when there was a recurrence. Between January 17 and 26 he received 47 milligram hours of radium. On Feb. 4, 1930 there was tenderness under the scar, which was stiff, and massage was recommended. On December 13 Dr. M. R. Caro found no surface evidence of recurrence. The bone at the external angle of the orbit felt roughened.

On Dec. 27, 1930 and Jan. 10, 1931 he received one unit of roentgen therapy (350 roentgens). The eye was protected by a sheet of molded lead. On Feb. 7, 1931 a roentgenogram of the left maxilla showed a slight defect, which was not due to carcinomatous metastasis. On June 17, Dr. C. M. Epstein excised the scar and as much tissue below and external to it as possible for histologic examination.

At the operation there appeared to be a recurrence down to and along the orbital wall. Histologic examination proved this to be a squamous cell carcinoma.

Between July 17 and Oct. 20, 1931 the patient received a total of 300 milligram hours of radium and 1,750 roentgens. Biopsy on several occasions in the first three months of 1932 showed no malignant growth, but that on April 26, 1932

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4. Dr. McEwen's (deceased) record does not state whether roentgen rays or radium was used, the exact dosage or whether the eye was protected.

showed the bone to be involved. In May 1932 three 2 mg. radium needles were inserted, and in May 1933 three 4 mg. needles were used, the latter to the extensions in the soft tissues of the cheek. In June 1933 Dr. C. M. Epstein resected the left upper jaw and did a curettement of the left maxillary antrum. A plastic operation to repair the defect was done on May 15, 1934, by Drs. Epstein and Samuel Salinger. After this operation there was a ½ inch (1.3 cm.) opening into the left antrum, and the exposed turbinates could be seen. On Sept. 8, 1934, May 14, June 9, Aug. 16 and Sept. 22, 1936, and on March 3, June 14 and June 25, 1937, further diathermy resections and plastic repairs were performed by the same surgeons. On Jan. 15, 1938 erysipelas of the face developed. On January 29 the patient had a cerebral hemorrhage, with complete left hemiplegia. On February 4 lobar pneumonia developed, and on February 9 the patient died. Autopsy was not done.

Examination of the Eye.—On May 27, 1936 vision in the right eye with a + 3.00 D. sphere was 8/10 — 3; vision in the left eye was limited to the counting of fingers at 2½ feet (75 cm.), which no lens improved. The left lower lid was adherent to the bulbar conjunctiva just above the fornix. The cilia were inverted. There was a yellow secretion on the margin of the lid. The globe could be neither elevated nor depressed, and there was limitation of both abduction and adduction. The bulbar conjunctiva in its lower one-half was beefy and chemotic. The left cornea was clear. The anterior chamber was deep. The pupil was 3.5 mm. in diameter, was regular and reacted normally to light and in accommodation. In the temporal one-third beneath the anterior lens capsule was a single vertical linear opacity. The left disk had an ampulliform excavation and a greenish pallor in the temporal two-thirds. The blood vessels bent over the scleral ring and were lost at 10 and 12 o'clock. The remaining blood vessels were all pushed to the nasal one third of the disk. With the Schiötz tonometer the tension was 30 mm. of mercury. Aside from a small triangular superficial scar extending 2.5 mm. into the cornea between 11 and 1 o'clock, the right eye was entirely normal. On July 13 there was further limitation of motion of the globe. The floor of the left orbit was partially absent. The lower lid was absent, and the skin was inverted and adherent to the orbital rim. There were marked congestion and chemosis of the lower one half of the bulbar conjunctiva. The globe was otherwise unchanged.

On September 28 the skin of the left upper lid was edematous, and the conjunctiva of the entire globe was chemotic. The lid was adherent to the bulbar conjunctiva at its temporal and nasal angles. On March 1, 1937 the upper lid was more edematous, and the skin was injected and more adherent to the bulbar conjunctiva. All the conjunctiva of the lower lid, fornix and bulb as far as the lower border of the internal and external rectus muscles was absent, and the inferior rectus muscle appeared only as a short 5 mm. stump attached to the globe. On June 10 the skin of the left upper lid was red, edematous and entirely adherent to the bulbar conjunctiva below the cornea, so that the cornea could no longer be seen. The tactile tension at this time was 3 +. The right eye was unchanged. On June 14 the globe was enucleated. At the time of the operation an artery at the external angle required a suture to control hemorrhage. The friable skin at the external angle was torn but was repaired with a silk suture. There was prompt healing of the conjunctiva.

Examination of the Enucleated Eye.—The enucleated globe was placed in a 4 per cent solution of formaldehyde for one hour and was then transferred to Held's solution and fixed for twenty-four hours.

It displaced 9 cc. of 50 per cent alcohol and measured 24 mm. vertically and horizontally and 24.25 mm. anteroposteriorly. The corneal epithelium was denuded between 10 and 3 o'clock (artefact). The remainder was smooth and glistening. Involving the inferior rectus and inferior oblique muscles was a firm cartilaginous mass, firmly attached to the sclera. This lay 8 mm. inferotemporally from the

Fig. 1.—Pectinate ligament with the spaces of Fontana containing pigment.

optic nerve and was 4 mm. in diameter. The tissue mass involved the inferior rectus muscle to within 8 mm. of its insertion and the inferior oblique muscle to within 6 mm. The latter was thin, taut and fixed by the mass to the sclera. The mass was yellowish gray. The optic nerve cut on the oblique measured 10 mm. in length and had a diameter with its sheaths of 2 mm. The remainder of the sclera was pearly white. The inferior vortex vein could not be located and was probably covered by the tumor mass.

A large calotte, measuring 23.75 mm. anteroposteriorly and 24 mm. horizontally, was removed above. The cut surface of the globe permitted a view of the

anterior chamber, which measured 5 mm. horizontally and was 0.5 mm. deep. The sclera measured 1 mm. in thickness. The choroid was everywhere in situ. The lens was in situ and had a golden sheen; its zonular fibers appeared to be normal. The retina was detached, except for 1 mm. around the optic nerve, leaving a 3 to 5 mm. empty subretinal space. It was uniformly gray. The

Fig. 2.—Pectinate ligament with depigmentation showing the spaces of Fontana.

cavum oculi was only partially filled by a filmy gelatinous vitreous attached by a few strands to the retina and optic nerve. The partially exposed optic nerve had a definite glaucomatous cup. The ciliary processes appeared whitish. The inferior calotte measured 16 mm. anteroposteriorly by 16.25 mm. horizontally and revealed the same structures as the superior, except that the anterior chamber was not exposed and the plain part of the ciliary body had been cut across.

Eight hundred and sixty-five sections were cut at between 14 and 16 microns. Every tenth section was stained with hematoxylin and eosin. Several sections were stained with Mallory's, Van Gieson's, Pal-Weigert's, Verhoeff's, Masson's trichrome and Alfiori's depigmentation methods.

Essential Microscopic Changes.—Cornea: The epithelium in its thickest portion was five to six layers of cells thick and at its maximum width measured 0.081 mm. In a few sections it was reduced to a single layer of cells and was absent due to artefact in parts of several sections. The basal cells were almost square, though some were columnar. There were a few clear spaces between cells. The cells themselves were poor in cytoplasm and their nuclei granular. Those cells
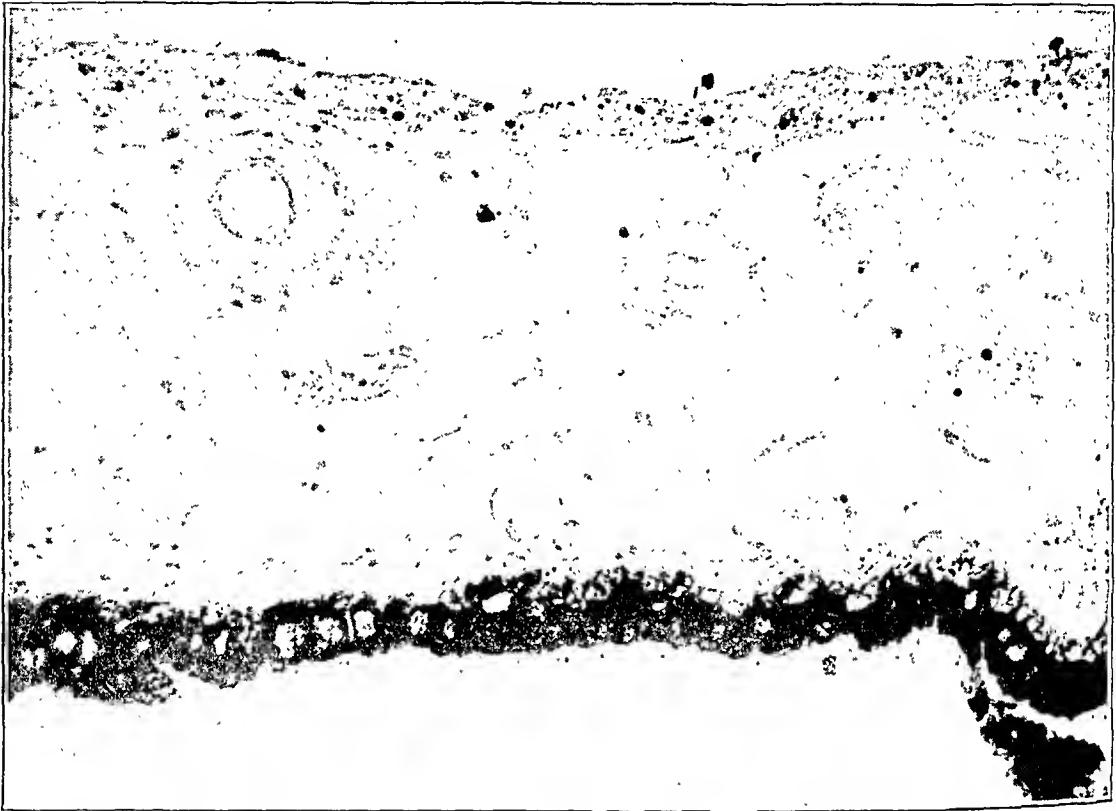
Fig. 3.—Iris showing rarefaction of the posterior pigment layer and pigment on the anterior surface.

just above the basal cell layer were narrow and flattened and contained oval nuclei. The outer layer was thin and flat and had elongated oval nuclei with occasional vacuoles. Bowman's membrane was granular and indistinct in its outer one-half beneath the area of greatest epithelial destruction. In most sections the substantia propria appeared normal, though in some the fixed cells were poorly stained. The endothelium was normal for the most part; in other places the cytoplasm was granular and the nuclei fragmented. In many sections there was fine, dustlike pigment on the endothelium near the angle of the anterior chamber.

Anterior Chamber: The anterior chamber was of varying depth, being deepest in the center, where it measured 1.39 mm. There was a slight amount of fibrinous material on the back of the cornea in a few sections and over the iris in two. There was scarcely any free pigment in the anterior chamber.

Pectinate Ligament: Not all the fibers of the pectinate ligament were sclerosed, though some fibers seemed slightly thicker than others; the nuclear fibers stained more poorly, and many of the spaces of Fontana were narrow. In every section the spaces of Fontana contained granular brown pigment. The canal of Schlemm was normal and did not contain any pigment. The pigment found in the
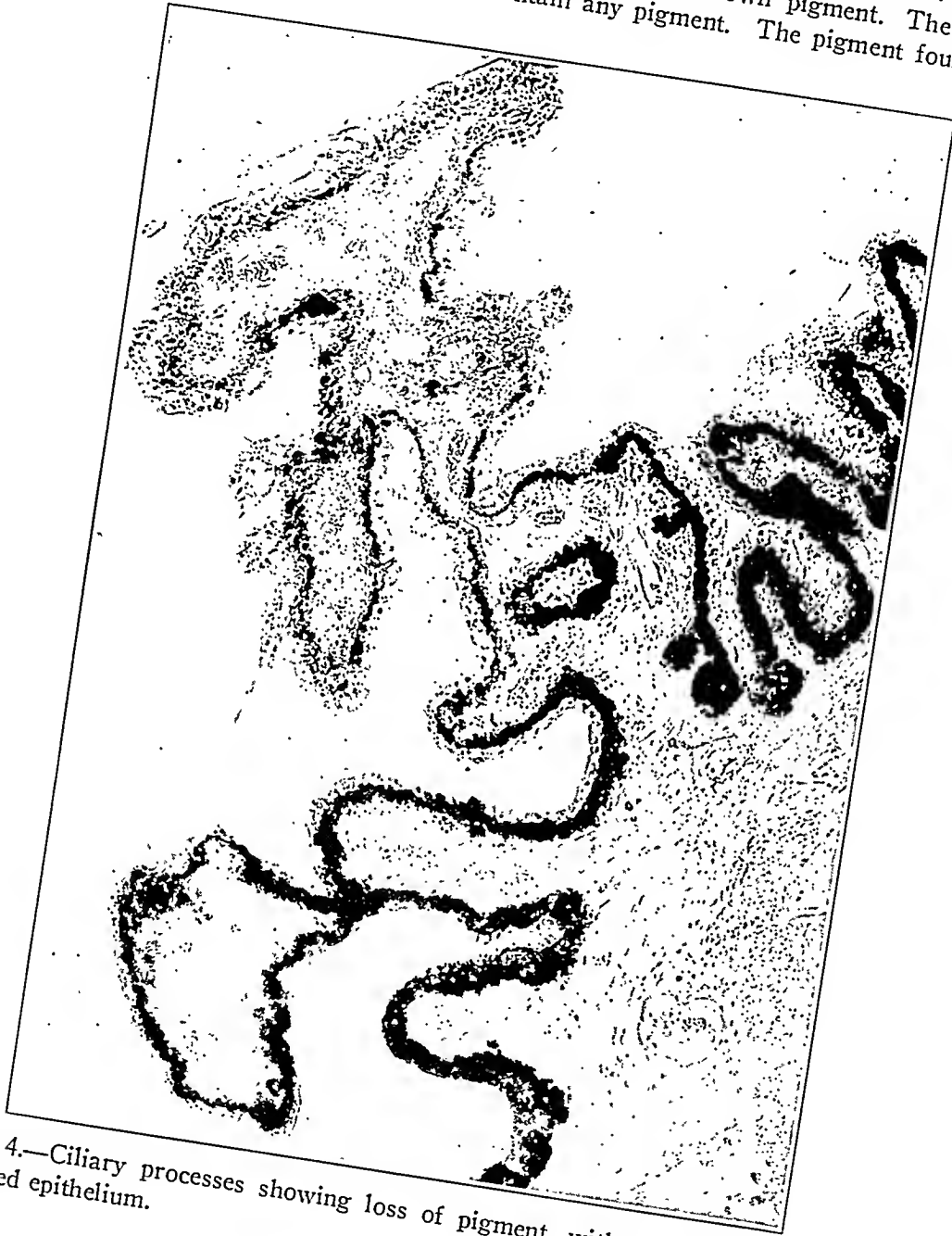
Fig. 4.—Ciliary processes showing loss of pigment, with changes in the non-pigmented epithelium.

angle of the anterior chamber was of irregular shape and size. It varied from single grains to clumps of granules which lay on the fibers of the pectinate ligament and in the spaces of Fontana. That it was not artefact is shown by its presence in every section. It was dissolved with the Alfiori depigmentation method. The remainder of pigment at the angle was scattered like dust on the endothelium (figs. 1 and 2). Iris: The iris was thin and rarefied throughout. Crypts appeared to be normal. There was almost no chromatophore pigment, and there were only a few clump cells. The pigment which covered the anterior surface of the iris was

fine and granular, and it was rare to find even a well formed clump cell here or near the angle of the anterior chamber. On the posterior surface the pigment was vacuolated and granular because of its dispersion. The blood vessels of the iris appeared to be normal. There were no anterior or posterior synechiae. Dilator and sphincter muscles were normal. In one area the pigment just behind the sphincter

Fig. 5.—Pigmented area of the choroid showing its invasion by tumor cells.

was almost absent, due to a disturbance of the capillary bed (section 170). In section 120 there was only a single layer of pigment on the posterior surface of the iris. Extending from sections 150 to 180, there was an oval, honeycombed, pigmented area at the root of the iris connected with a posterior layer of pigment. This measured 0.12 mm. anteroposteriorly by 0.69 mm. radially by approximately 0.33 mm. vertically (fig. 3).

Ciliary Body: The ciliary muscle was approximately normal in all but a few sections, where there appeared to be a pressure atrophy. In most sections there was pathologic depigmentation of the ciliary processes, with poor staining and some vacuolation of the unpigmented epithelium. The lens capsule and lens epithelium were everywhere intact, and there was no demonstrable cataract (fig. 4).

Choroid: The choroid was shrunken and thin throughout from fixation in formaldehyde, except in the area of metastasis. The choroidal blood vessels showed moderate sclerosis. The pigment epithelium was rarefied and granular.
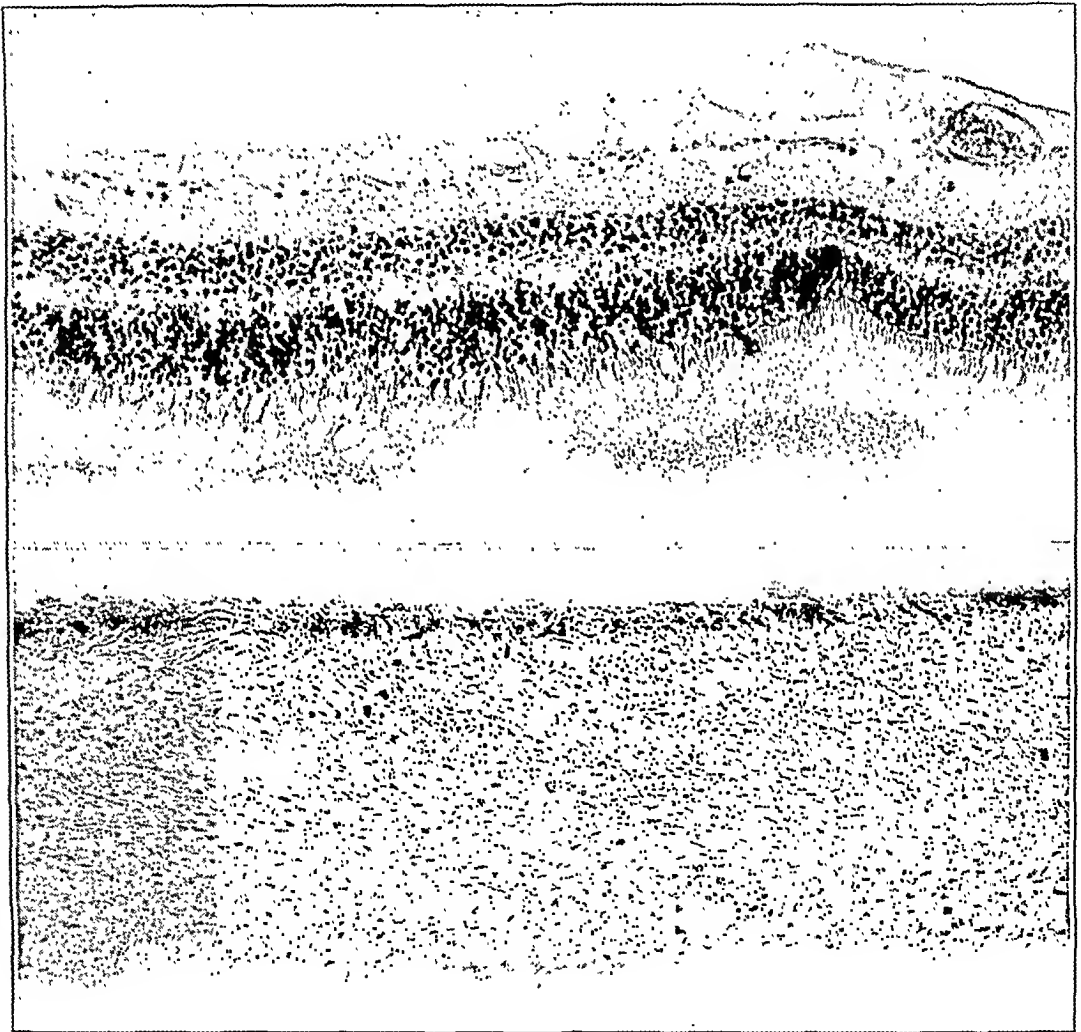
Fig. 6.—Depigmented area in the choroid showing the tumor cells.

There were many proliferations of the lamina vitrea. The pigment over these was especially granular. The choroid was adherent to the retina in several places. The pigment epithelium was flattened and granular but still present in these areas, and there were no breaks in the lamina vitrea. Opposite the external tumor, the choroid contained a dark brown granular mass which measured 3 mm. horizontally by 2.97 mm. anteroposteriorly. A tumor began about 12 mm. behind the ora serrata. When depigmented by the Alfiori method, this growth was seen to be a squamous cell carcinoma by direct extension through the sclera.

Retina: The retina was atrophic. Nuclear layers stained normally. In the area opposite the choroidal tumor the internuclear layer was vacuolated and two and a half times as wide as the outer nuclear layer. The retina was adherent to the choroid in several localized areas. Here the rod and cone layer was granular and vacuolated, and the epithelium pigment was thin or absent. The ganglion cell layer was thin, granular and vacuolated. The walls of the blood vessels were of about normal thickness; none were twice the thickness of their lumens. There were many cysts near the ora serrata on both sides (figs. 5 and 6).

Optic Nerve: The optic nerve was pathologically cupped, and its nasal side was even undermined. At the scleral ring the cup measured 0.78 mm. and the level of the lamina cribrosa 0.91 mm. The nasal side of the cup was 0.83 mm.
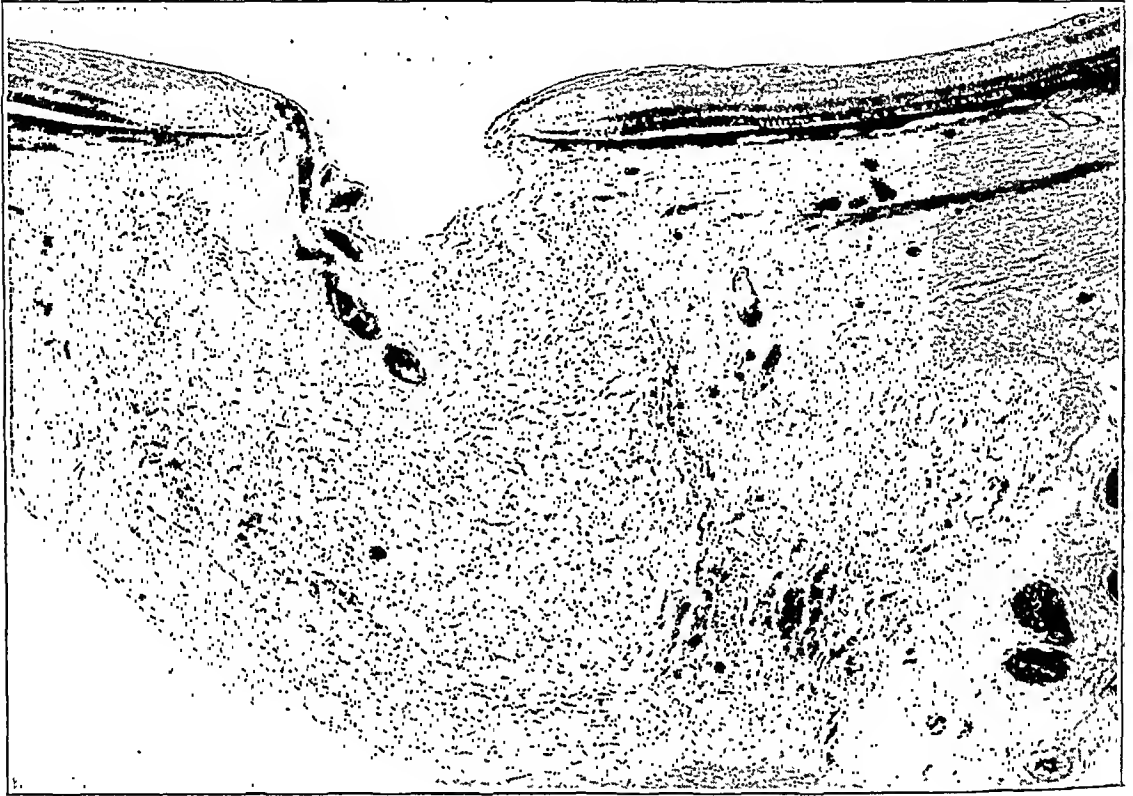
Fig. 7.—Optic nerve showing the glaucomatous cup with a small area of medullated nerve fibers; periphery of the left side (Pal-Weigert stain).

deep and its temporal side 0.51 mm. Its floor reached the lamina cribrosa. In section 390 the floor of the excavation was bridged by a blood vessel from the nasal side. The Pal-Weigert stain in section 469 showed only two areas stained dark blue. One near the sclera measured 1.15 mm. by 0.97 mm., and another area along the edge of the nerve was 0.16 mm. wide by 1.64 mm. long (fig. 7).

Tumor: The tumor reached its maximum size in section 730. It measured 2.59 mm. anteroposteriorly by 10 mm. horizontally by 2.12 mm. vertically. Section 190 showed a beginning small, round, inflammatory cell infiltration of the inferior oblique muscle. Section 360 was the first section which showed the tumor cells in the muscle. Section 450 showed the beginning involvement of the episcleral tissue by the growth. Section 680 showed beginning invasion of the sclera with

tumor cells along the blood vessels and lymphatics, and in section 710 the sclera was definitely thickened by the invading mass. There was hemorrhage between the tumor and the sclera. In section 770 the sclera was invaded for 0.06 mm. In section 780 there were epithelial pearl nests in the sclera. There were lymph spaces containing blood, new blood vessels and a small, round, inflammatory cell infiltration in the invaded sclera as well as tumor cells.

The tumor itself was made up of squamous cells with many mitotic figures invading and attached to the muscle. Scattered hyalinized epithelial cells were present; there were also some new blood vessels and groups of small, round cells about the vessels (fig. 8).
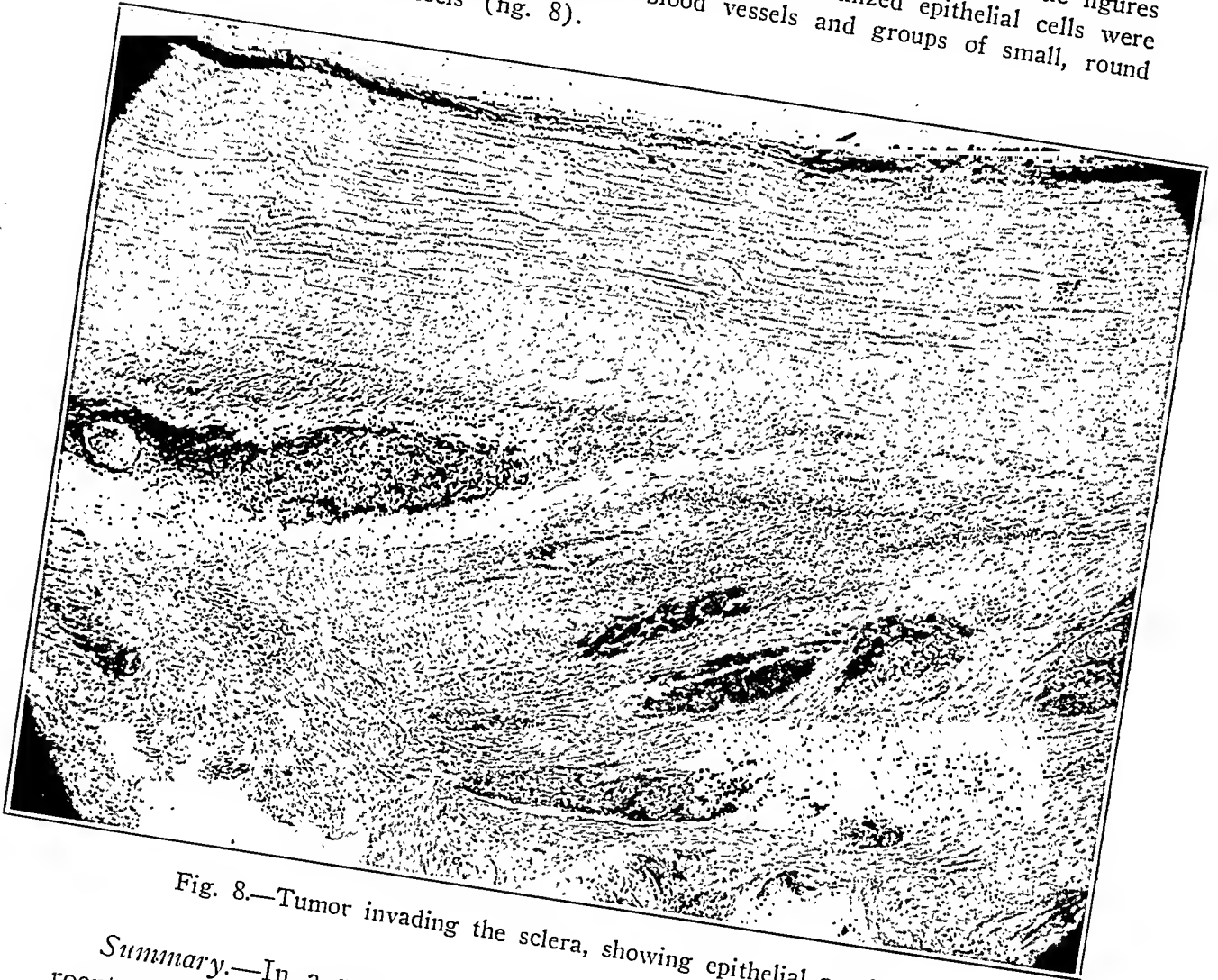
Fig. 8.—Tumor invading the sclera, showing epithelial pearls.

Summary.—In a man, aged 62, who had received large doses of roentgen rays and radium, much without protection, unilateral glaucoma developed.

Histologic study revealed thinning and destruction of corneal epithelium and some damage to the endothelium, atrophy of the ciliary processes and marked dispersion of pigment from the ciliary processes and posterior surface of the iris, with blocking of the spaces of Fontana and the anterior surface layer of the iris, with a resultant glaucoma. There were complete and total glaucomatous atrophy of the optic nerve, moderate sclerosis of the choroidal vessels and atrophy of the ganglion

cell layer of the retina. Invasion of the sclera and choroid by the squamous cell carcinoma was incidental and must have occurred late in the disease.

<div align="center">COMMENT</div>

Was the glaucoma due to direct action of the rays on iris and ciliary body pigment, causing its dispersion?

The fact that the blood vessels were little changed from those of a patient of the same age with normal tension would indicate that vascular changes played no role in this case.

Corneal epithelium is avascular, yet roentgen and radium produced severe damage in this and in all reported cases as well as in rabbits' eyes. It would seem that alterations from irradiation are not secondary to vascular changes.

In Birch-Hirschfeld's cases, both with and without glaucoma, there was a similar change in the pigment epithelium as well as in the blood vessels of the iris and ciliary body. Birch-Hirschfeld expressed the belief that the pigment disturbance was secondary to the vascular change, yet in his experimental work on rabbits he described a gushing forth of pigment of the iris and ciliary body without vascular change. It is true that pigment disturbance is seen in cases of chronic glaucoma of unknown causation, but in most of these there are anterior synechiae. It is true that in some cases of glaucoma only sclerosis and some pigment in the spaces of Fontana with deep anterior chambers are observed. These are not the usual findings, however, and most often the other eye also has glaucoma.

Whether the damage to the ganglion cells was due to irradiation or was a result of glaucomatous pressure is also difficult to decide. The vacuolation of these cells, their shrinkage, hyperchromatosis of their nuclei and dispersion of the chromatin substance occurred in the retinas of rabbits. These changes occurred in areas near blood vessels and in others free from retinal vessels, so that they were not dependent on vascular changes. The changes occurred clinically at a slower rate than those in experimental animals. The same type of change occurs clinically in cases of quinine and methyl alcohol poisoning and is seen in some eyes after death, so that they may have been due to direct action of the rays on the retina. However, similar changes can be due to glaucomatous pressure atrophy.

Why irradiation produces cataracts without glaucoma in some eyes and glaucoma without lenticular changes in others or both conditions is not known. In still other eyes with normal lenses or with aphakia, retinal atrophy may follow irradiation. It is possible that there is a selective action of the rays for certain structures, but such selectivity has neither been explained nor can it be predicted.

CONCLUSION

A case in which glaucoma followed radiation therapy is presented in detail. Minor doses of roentgen rays were given in 1914, 1929 and 1930 and large doses in 1931, 1932 and 1933. The diagnosis of glaucoma was made on the first visit of the patient in 1936. There was no tumor in the eye when the fundus was visible. The glaucoma was unquestionably present before the choroid was invaded. The choroidal involvement consisted of a slightly less than 3 mm., almost round tumor. The right eye remained normal. The outstanding pathologic change was the breaking up of anterior uveal pigment epithelium and its dispersion over the anterior surface of the iris and in the spaces of Fontana, with little vascular change and no synechiae. In the 3 recorded cases and in my 2 cases which were briefly outlined, as well as in the last reported case, similar alterations of anterior uveal pigment were found. It is assumed that the pigment disturbance was due to the roentgen rays and that the glaucoma in the last case was of mechanical origin due to blocking of the flow of aqueous from the eye.

Drs. Caro and Epstein gave me permission to use their records; Dr. E. V. L. Brown helped with the pathologic study and Mrs. A. Carroll prepared the specimens.

DISCUSSION

Dr. Walter E. Camp, Minneapolis: I thought that as long as irradiation is being considered as the cause of glaucoma, it might be well to summarize the present knowledge of how irradiation affects the tissues of the eye.

Antenatal irradiation to the mother may produce questionable anomalies of the eye and congenital cataract. Rapidly growing eyes of young animals irradiated soon after birth show: (1) retardation of growth in the size of the globe (there being marked retardation in all the tissues of the globe for a considerable time, with greater retardation the younger the animal) and (2) marked and early cataractous change in the lens. It seems that the lenses of young persons are much more sensitive to irradiation than those of older persons.

The conjunctiva and lids are more sensitive at all ages than are the remaining structures of the eye or the surrounding skin of the face. To me, it was enlightening to know that the lids are more sensitive than the skin around the face.

The sensitivity of the cornea is next in order. The iris is next in order of injury, which consists of myosis, disturbance of iris pigment and degeneration and swelling of the endothelium of blood vessels. The myosis is resistant to drugs and may even be permanent. Apparently the damage to the blood vessels develops late and after a large dose. The retardation of pigment formation is constant and the iris is affected only by large doses of radiation, both in young experimental animals and in clinical patients.

The lens of adults is quite resistant to irradiation. The retina is least sensitive. Pathologic changes frequently reported are usually due to postmortem change. The retina, like the entire central nervous system, is extremely resistant to irradiation.

It would appear from Dr. Bothman's slides that glaucoma possibly caused by irradiation was being dealt with, although one has to be careful in ruling out any other possible cause for the condition.

From a study of the material available, it is apparent that when the uveal tract is damaged by irradiation it is the uveal pigment that is chiefly affected. In the fetus and infant pigment formation is greatly retarded. It is probable, as Dr. Bothman emphasizes, that it is this dispersion of pigment rather than sclerosis of the meshwork of the iridocorneal angle that accounts for the chronic glaucoma. In view, however, of the invasion of the orbit and globe by a neoplasm, as in this case, one should hesitate to attribute the glaucoma to irradiation alone.

Dr. Georgiana Dvorak-Theobald, Oak Park, Ill.: I wish to present several slides with a normal trabeculum, showing (1) openings from the anterior chamber into the intertrabecular spaces, (2) the inner canals of Sonderman connecting the intertrabecular spaces with the canal of Schlemm and (3) the external collector channels which connect the canal with the anterior ciliary veins. Aqueous humor reaches the canal of Schlemm by way of the intertrabecular spaces and the inner canals. When the intertrabecular spaces become occluded, increased intraocular tension results. The occlusion may be due to a swelling and sclerosis of the trabeculae or to a blockage of the intertrabecular spaces by foreign substances.

In the specimen presented by Dr. Bothman, the intertrabecular spaces are completely blocked with degenerated pigment, derived from the pigment epithelium of the iris and ciliary body, which are atrophic. The trabecular fibers are sclerosed, hazy and stain poorly.

Disturbance caused by irradiation may be due to: (1) hyperemia and subsequent inflammation, (2) obliteration of the blood supply and atrophy of the adjacent tissues and (3) direct action on the nuclei of the pigment epithelial cells themselves.

When the nutrition of uveal pigment epithelium is interfered with, these cells may proliferate, disintegrate and migrate.

The pathologic process in this eye is such as is found in the late stage of severe glaucoma, secondary to pigmentary degeneration without regard to causation.

MELANOSARCOMA OF CHOROID

REPORT OF A CASE WITH UNUSUAL FEATURES

EDWIN NEWMAN BEERY, M.D.
BROOKLYN

P. N., a white man 66 years old, was examined in my office on Dec. 21, 1938 for an enlargement of the right eye of nine months' duration. In 1928 he had undergone iridectomy on this eye for secondary glaucoma at the New York Eye and Ear Infirmary; permission for enucleation was subsequently refused. Past and family histories were irrelevant; nothing could be learned regarding the primary ocular condition. From the time of this hospitalization to the onset of the present illness the right eye had been blind but quiet. The first symptom noticed was a rapid increase in the size of the eye; this was followed by protrusion and recently by occasional pain and bleeding.

Examination disclosed a blue-red, blackened globular mass, approximately 3 by 3 cm. in size, which was firm and nontender. Its presenting surface had a small area of superficial necrosis. The mass completely filled the interpalpebral fissure and posteriorly contracted into a thick stalk, which passed intraocularly; it appeared that the growth had originated from within the eyeball and had pushed through at the corneoscleral juncture to replace the anterior chamber and cornea. On transillumination, it was completely dark.

Examination of the left eye showed a severe argyria and a few opacities of the vitreous; vision with correction was 20/30.

Preoperative study in the Brooklyn Eye and Ear Hospital failed to reveal any systemic disease. This study included: urinalysis and roentgen examination of the lungs, mediastinum, abdomen and optic canals. A general physical examination by Dr. Alfred Ingegno disclosed a chronic bronchitis of little importance. Digitally, the prostate was normal, the edge of the liver was smooth and there was no generalized glandular enlargement.

After consultation with the late Dr. Edwin M. Beery, a subtotal exenteration (including the periosteum but sparing the lids and their attached palpebral conjunctiva) was effected on December 22, with the patient under general anesthesia. Postoperative irradiation was decided against after consultations with Dr. Nathan T. Beers, of Brooklyn, and Dr. Hayes E. Martin, of New York.

One month after operation nodules were noted on each lid; recurrences were feared and specimens were taken for biopsy on three occasions. Histologically, each specimen showed a surface covering of squamous epithelium with underlying scar tissue containing clumps of black pigment; reference to the severe argyrosis of the eye that was not operated on identified the pigment as reduced silver and not melanin.

Grafting of the orbit was not necessary owing to rapid extension of the epithelium of the palpebral conjunctiva, which had been spared at the exenteration; six weeks after operation the cavity was completely relined with epithelium. Rapid contracture of the cavity appeared but was effectively controlled by the insertion of a mold of dental plastic compound under pressure dressings. A pros-

Fig. 1.—Anterior and lateral aspects of the mass on Dec. 21, 1938.

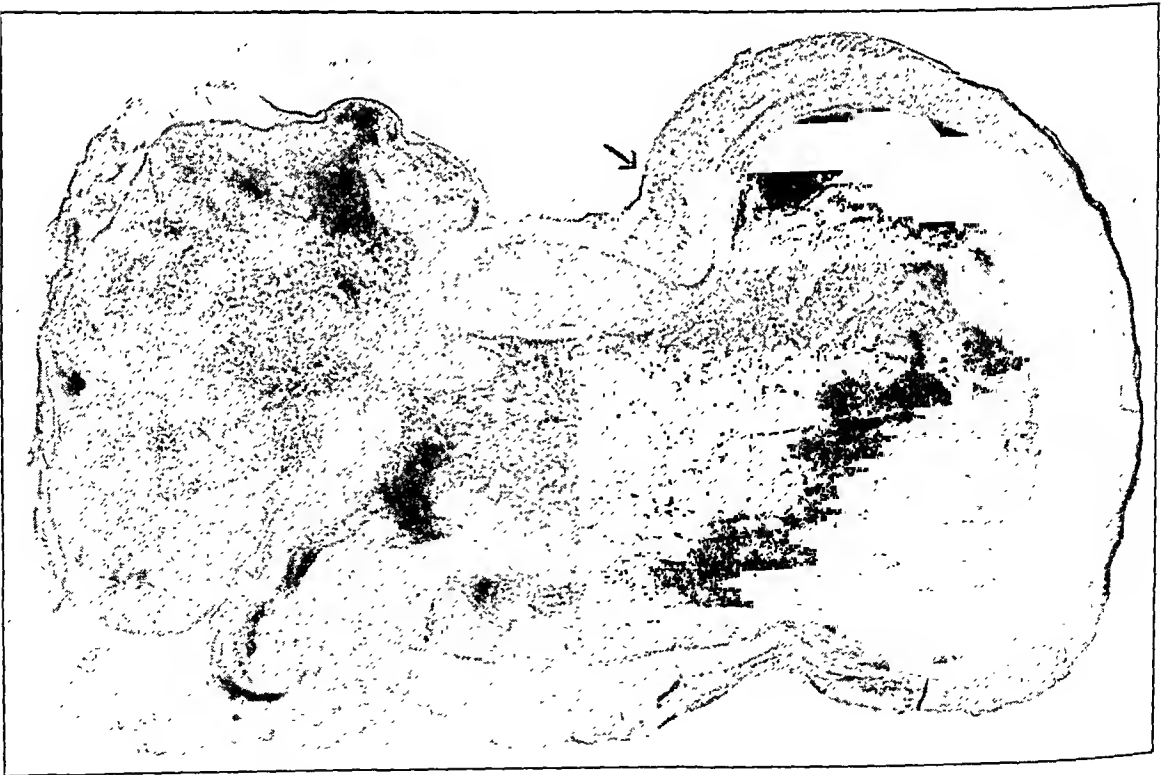Fig. 2.—Operative specimen on Dec. 22, 1938.

Fig. 3.—Half globe pathologic specimen; × 40. Note the strip of sclera in the upper center. The arrow indicates the juncture of stratified squamous epithelium and a refractile substance which may be corneal residue. Between this and the anterior extremity of the sclera, uveal pigment is found.

thesis was supplied two months postoperatively, and the patient is now well and happy one year after operation and is completely satisfied with the cosmetic result.

Dr. Arnold J. deVeer examined the operative specimens, which included the globe and portions of the orbital contents. The latter were histologically free of involvement and failed to show any intraorbital spread of the tumor. The half globe specimen showed that the eye had been completely destroyed; it was replaced by the actively growing tumor tissue except near the equator, where one found a 1 cm. strip of sclera and, adjoining its anterior extremity, remnants of uveal tissue and glass membrane. The tumor was characteristic of melanosarcoma with its mixed content of spindle and polyhedral cells; there was a large amount of pigmentation throughout, and many centers of necrosis were found.

COMMENT

This case definitely falls into Fuchs's [1] third stage of the disease in which, after a period of increased tension, the tumor breaks through the sclera and grows outside the eyeball. One may only conjecture as to the duration of the malignant condition: Subjectively, it had been present nine months; lack of antecedent clinical records and follow-up study prevented one from knowing if it was present at the time of original iridectomy ten years before.

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1. Fuchs, E.: Text Book of Ophthalmology, translated by A. Duane, ed. 7, Philadelphia, J. B. Lippincott Company, 1923, p. 725.

FURTHER EVIDENCE OF CHANGE IN POSITION OF THE EYEBALL DURING FIXATION

GEORGE E. PARK, M.D.

CHICAGO

AND

RUSSELL SMITH PARK, PH.D.

RICHMOND, KY.

The general attitude of ophthalmologists heretofore has been to regard monocular and binocular vision as being dependent on a rather fixed peripheral mechanism in which the visual axis, the position and symmetry of the lens and the position of the eyeball in Listing's plane are not considered to change. The graphic illustrations which are used even in the most recent textbooks and periodicals teach this point of view.

THE EARLIER CONCEPTS

The much discussed and exactly located center of rotation of the eye is still debated by ophthalmologists. On the supposition that such a center exists, Johann Benedict Listing established the plane which bears his name. It is defined as a stationary plane which passes through the center of rotation of the eyes in a vertical transverse position. He concluded that the eyeball in its rotation, irrespective of direction, would have to rotate about an axis within this plane.

On this postulate he established his famous law of ocular rotations about a hundred years ago, stating that "when the line of fixation is brought from its primary position into any other position, the torsional rotation of the eyeball in this second position will be the same as if the eye had been turned around a fixed axis perpendicular to the initial and final directions of the line of fixation." Helmholtz, in interpreting this law, stated that the line of regard does not necessarily proceed from the initial to the final position along a straight line or that the eyeball really does not turn around a fixed axis. On the contrary, the passage from the initial to the final positions may be accomplished in any way. And yet Helmholtz, in discussing the "plane of reference," made use of a line which joins the centers of motion of both eyes. But according to Donders' law, the final position is invariably the same.

Maddox in his book depicted a complicated conical design to explain false torsion in which he used a fixed center of rotation and also a definitely fixed plane, i. e., Listing's plane. In discussing the index of torsion, he stated that since the eye is an optical instrument he believed the index of torsion should be an optical one.

Therefore, Listing's law, if it is to be interpreted with its presumptive mathematical accuracy, certainly postulates a fixed center of rotation of the eyeball. This idea is a feature of the mathematical concepts which characterize the earlier opinions. These opinions are generally accepted by contemporary ophthalmologists who attempt to make the theory of neuromuscular functions fit such an exacting pattern.

TRANSLATION OF LISTING'S LAW

In 1933 [1] we published a report of our investigation on the position of the center of rotation of the eyeball, at which time we reached the conclusion that the center of ocular rotation is not fixed but moves along a curve a variable distance, from 1 to 1.6 to 0.89 mm., nasalward from the visual axis and always on a line perpendicular to the visual axis at O (fig. 1 A and B).

Also, the distance O-O' varied. As the angle of the axis takes the position at 39 degrees nasalward, the distance is 14.7 mm. At 4 degrees nasalward the distance from O' to O is only 13.9 mm. As the visual axis swings to 38 degrees templeward, the distance is diminished to 12.9 mm. (fig. 1 C). In the construction of the instrument used for this study a vertical hair was placed through the optic axis of the tube which appears in the photograph. During the photographing, this cross hair was set at 13.33 mm. from the arc center of the instrument or, in other words, from the visual center of the eye, point O. The photographs were made at right angles to the visual axis, while the angle of fixation was at the position designated. The point O, or the visual center of the eye, is understood as being the point which is fixed within the socket through which the visual axis passes at all times while the eye is moving in the horizontal plane but not fixed in relation to the eye. O' is the position on the cornea through which the visual axis passes.

Since there is no fixed center of rotation of the eye, it is impossible to establish a stationary plane corresponding to Listing's theoretic plane. Therefore, the observations and calculations which have been made on this assumption would necessarily be incorrect.

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1. Park, R. S., and Park, G. E.: The Center of Ocular Rotation in the Horizontal Plane, Am. J. Physiol. **104**:545-552 (June) 1933.
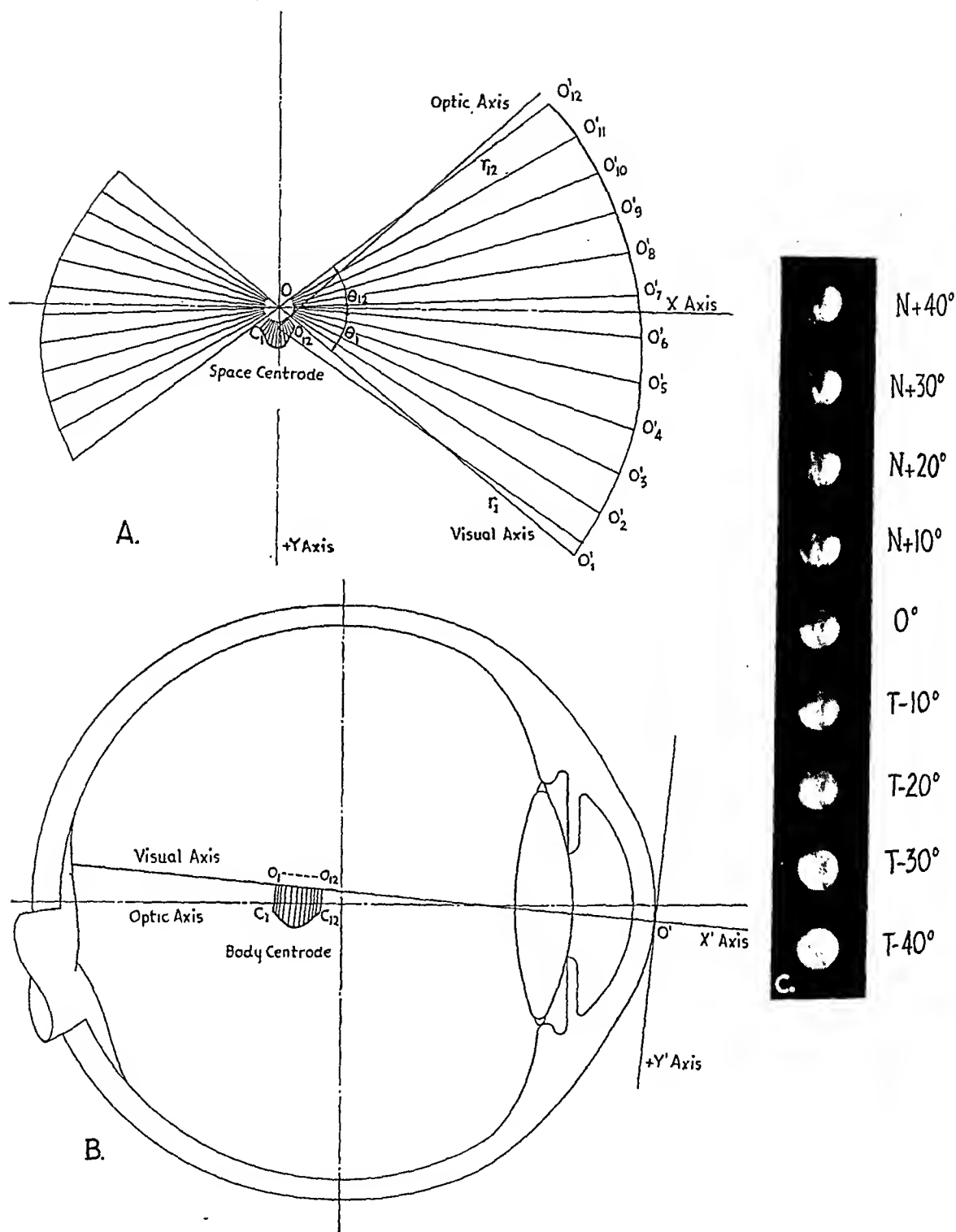
Fig. 1.—*A*, diagram of the positions of the visual axis in the horizontal plane, showing the position of the space centrode and of point *O*. *B*, diagram of the eyeball in the horizontal plane, showing the visual axis, the position of the body centrode and the points at which the space centrode intersects the body centrode, C_1 to C_{12} during a horizontal excursion of the eye between O'_1 and O'_{12}. *C*, photograph showing the position of the corneal vertex relative to the fixed vertical wire of the eyepiece during an excursion between 40 degrees templeward and 40 degrees nasalward.

A NEW CONCEPT DURING STATIONARY FIXATION

In 1936[2] a report was made on an investigation of the angular relation of the visual and optic axes of the eye. This optic axis is defined as the axis of the cornea which intersected the visual axis at or near the visual center of the eye, point *O*. We have called the angle between these two axes the physiologic angle. It is generally known that these axes seldom correspond. For those observations a specially constructed instrument, the precision anglometer,[3] was utilized to establish a primary fixation position wherein the visual axis of the eye was coincident with the optic axis of the telescope. This primary position was essential before proceeding with an observation.

With some subjects this physiologic angle would remain fixed for several minutes, or until they changed their point of regard momentarily, when the change would be noticed. Even at times there could be no shift demonstrated. With others, the angle would remain stationary for only a few minutes, when it would either begin to diminish or to increase to a certain limit, where it became fixed for a short period; it would then reverse and continue to the original position and even beyond. It could at any time become momentarily fixed within the limits of its excursion. With other subjects there was almost a continuous randomness present, with only a short pause made at definite positions in the excursion, even approaching the appearance of a mild nystagmoid movement. Some subjects showed a much greater limit of variation than others. There are no norms, not even for the same person.

In attempting to establish a control of the phenomenon, physostigmine salicylate, homatropine hydrobromide and atropine were used. Observations were made immediately after the instillation.

Invariably, immediately after the instillation of physostigmine salicylate the angle became much smaller; it would remain for a short time at this size and then increase beyond the original amount. After three or four instillations of a 0.25 per cent solution of physostigmine salicylate it was noticed that the corneal reflex, moving at random, would gradually approach the horizontal line, even rising above it, but at once would drop below again. Eventually, with marked randomness (and sometimes requiring an hour or so) the reflex would appear at the intersection of the horizontal and vertical lines of the scale at the eyepiece of the instrument. At that time the physiologic angle had become

2. Park, G. E.: An Investigation of the Angular Relation of the Visual (Visierlini) and Optic (Corneal) Axes of the Eye, Am. J. Ophth. **19**:967-974 (Nov.) 1936.

3. Park, G. E.: The Precision Anglometer, Arch. Ophth. **15**:703-709 (April) 1936.

zero, varying perhaps from $+$ 1 or 2 degrees to $-$ 1 or 2 degrees, where it would remain.

With the instillation of homatropine hydrobromide, a different condition developed. Immediately after its instillation, the physiologic angle would undergo a change; sometimes it would increase and at other times diminish. The general randomness was similar to that noticed with the instillation of physostigmine salicylate, and in a majority of cases the angle would eventually approach zero. There were many exceptions to this, for in many cases the final result might be that the angle had increased from 6 or 8 degrees to 17 degrees, where it would remain more or less fixed. Apparently the angle did not change from one position to another so rapidly after the use of homatropine had become fully effective, especially if the eye was held in fixation. But if there was a change in the point of regard and the target was fixed again, at times a definite oscillation of the corneal reflex was observed, resulting eventually in a different angle between the optic and the visual axis. Atropine established a condition similar to that produced by homatropine.

In measuring aphakic eyes, another important observation was made. Some difficulties were experienced in establishing coincidence of the visual axis and the optic axis of the instrument on account of low visual acuity, but by allowing the subject to select the position which appeared to be the clearest, the physiologic angle would become zero without exception, provided postoperative refraction had secured practically normal vision.

Another check that was used was to move the instrument until the physiologic angle was brought to zero, at which time the subject would invariably report the most acute vision of the target within the circle, the zero position being reached without the knowledge of the subject, except as the position of the most acute vision.

The conclusions reached at that time were that in binocular foveal fixation it can be assumed that the resultant remains constant, that is, that the two foveas are kept steady under the central images; but it would be unreasonable, considering what is known about neuromuscular functions, to suppose that the flow of muscle effort, the muscular pattern, maintains the same line of direction and the same relative quantities at all times in an absolute sense.

If nothing else occurs, it is almost certain that innervation and contraction, both in the ciliary muscles and in the extrinsic muscles, shift from one group of muscle fibers to another, as they do in all muscles under continued effort. But it is likely that the changes are of a grosser character than that. Almost certainly the entire musculature shifts its line of force, so that the extrinsic muscles change the angle of

fixation and the ciliary muscles change the shape and curvature of the crystalline lenses, but with an uncanny coordination which maintains the same resultant, namely, the focusing of the central images on the two foveas.

Possibly the extrinsic muscles rotate the eye to approximately the point of fixation, and the ciliary muscle acts as what might be termed a fine adjustment for exact fixation by means of the change in the shape of the lens. In prolonged fixation it is possible that, due to innervation and contraction, the extrinsic muscles act to shift the fovea away from the image and that the ciliary muscle acts to shift the image to the new foveal position.

Conversely, it is also possible that the ciliary muscle, for the same reason, shifts the image and that the extrinsic muscles rotate the eye to bring the fovea beneath this new image position.

The theory of fixation by the extrinsic muscles only appears to be modified in this respect. Inversely, in an aphakic eye the ciliary muscle cannot exert this influence, and fixation is entirely accomplished by the extrinsic muscles.

The question as to which muscles originate the shift, the ciliary or the extrinsic muscles, and which compensate is difficult to answer, as we have mentioned before, for they are probably interchangeable.

The whole matter is undoubtedly one of adaptation and fatigue, plus an uncanny coordination to maintain a desired resultant. Varying conditions would seem to vary the role of originator and compensator between these muscles.

The described method of securing coincidence of the optic axis of the telescope with the visual axis is accurate to within a maximum error of ¼ degree. It can be easily recognized subjectively within that limit when the image has shifted from central fixation.

THE VISUAL AXES IN MOTION

During the observations which have been reported previously, the visual axis was held stationary. Since our observations seemed to involve such a radical departure from the orthodox theories, we decided to carry the research further and observe the functioning of the eye while the visual axis was in motion.

We possess not only our own evidence in support of our contentions but the observations of other investigators.

Hess[4] made a thorough investigation of the movement of the lens during accommodation and found that a downward movement occurs, as

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4. Hess, C., in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1929, vol. 12, p. 145.

described by Tscherning. Hess claimed that the lens sinks downward about 0.25 to 0.36 mm., but that the direction in relation to the pupil is dependent on the position of the head and that the movement does not occur when the iris is horizontal. He also observed in an eye into which physostigmine salicylate had been instilled, a maximum movement of 1 mm. when the head moved through an angle of 180 degrees from shoulder to shoulder.

Hess further observed a marked to and fro movement of the lens in a similarly treated eye with every movement of the head, the phenomenon disappearing after the instillation of atropine. This movement was most marked when the head was held backward. The lens seemed to make three or four oscillations after cessation of the side to side movement of the head.

Hess and several other observers noted irregularities in the border of the lens such as might be due to greater pressure on one part than on others. Hess observed that this wavy border became more uniform after the instillation of physostigmine salicylate.

He also observed a certain phenomenon which he believed was probably due to the possibility that the iris and ciliary musculature did not function simultaneously. In substantiation, he cited certain observations.

Peckham,[5] by using prisms in the base in or base out positions before a stereoscope, was able to carry the subject to almost diplopia while the latter still reported fusion or oneness. The eyes of the subject in overcoming a 10 degree prism moved through angles often less than half this amount, although occasionally they moved even too far to bring the foveas beneath the images. Hence, Peckham concluded that the fovea was 3 or 4 degrees from the ideal position. He observed, moreover, that when certain subjects were required to look successively without mirrors at two points on a large perpendicular field at a distance of 0.5 meter, although each point was placed equally distant from a midline (which should have required the same amount of convergence) there was as much as 4 or 5 degrees of difference between these two fixations.

Clark [6] in his work interpreted certain observations which he made thus: The eyes move at random sufficiently fast to cause a definite diminution of vision; convergence had no effect on fixation, and any position within an area of 1 degree to 1.5 degrees from the center of the fovea may be used to "fixate" a point. The randomness and irregularity are characteristic rather than the exception.

5. Peckham, R. H.: Foveal Projection During Ductions, Arch. Ophth. **12:** 562-566 (Oct.) 1934.

6. Clark, B. C.: An Eye-Movement Study of Stereoscopic Vision, Am. J. Psychol. **48:**82-97 (Jan.) 1936.

Besides these authors, McAllister,[7] Gertz[8] and Grim[9] reported definite movements of each eye when fixation was apparently stationary. Both Grim and Gertz found excursions of from 4 to 10 degrees when the eyes were fixed.

Burri,[10] in a report on the concept of abnormal retinal correspondence, pointed toward a dynamic plasticity rather than a static anatomic relation.

Bielschowsky,[11] in a recent paper, reported some observations which would indicate considerable fluctuation and dynamic variability. He also concluded that this condition is unstable and may change either spontaneously or in the course of time.

In the present article a study is reported which was made to show the relation of the excursions of the aphakic and nonaphakic eyes when reading similar material under similar circumstances. The ophthalmograph (fig. 2) was used in photographing the excursion of the eyes. In the standard form the lights serve to illuminate the reading card and to reflect light from the cornea for making the photographic record. As these lights are located at either end of the reading card, it is seen that when an ammetrope reads the card through his correction the recorded excursion is influenced by the action of the light from the lamps passing through the lens to reach the corneas and is again influenced after the reflection from the corneas by a second passage through the lens to reach the photographic film; the recorded excursion is therefore not the actual excursion of the eye. This objection was overcome by positioning a second pair of lights, *A,* at about the ocular level at the same separation as the standard lights. By the use of the half eye test lenses, *B,* light from the lamps now reaches the cornea above the reading lens and is reflected back toward the photographic film uninfluenced by the reading lens. Therefore, the recorded excursion is the actual excursion. By this means the actual excursions of all eyes, whether they are emmetropic, ammetropic or aphakic, are recorded irrespective of the sign or power of the necessary reading lens. Of course this recorded excursion of the eye is influenced by the sign and power of the reading lens, but it is a simple

7. McAllister, C. N.: The Fixation of Points in the Visual Field, Psychol. Rev. (supp.) **7**:17-53, 1905.

8. Gertz, H.: Ueber die Blickaberration und ihre Beziehung zur Netzhautcorrespondenz, Acta ophth. **13**:192-224, 1935.

9. Grim, K.: Ueber die Genauigkeit der Wahrnehmung und Ausführung von Augenbewegungen, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. (pt. 2) **45**:9-26, 1910.

10. Burri, C.: The Concept of Abnormal Retinal Correspondence, Arch. Ophth. **19**:409-424 (March) 1938.

11. Bielschowsky. A.: The Etiology of Squint, Am. J. Ophth. **20**:478-489, 1937.

matter to compute the amount of this influence and to determine the normal excursion of the eyes of any patient irrespective of whether reading glasses are worn or not. In this manner excursions of all eyes and their relation to each other are studied on a common basis.

This influence could not be ascertained by any adjustment of the instrument, and recourse was had to the computation of a factor pertaining to each dioptric power and sign of the lens by which the graphic excursions obtained when the patient was using reading lenses were multiplied to convert them to the normal excursions.
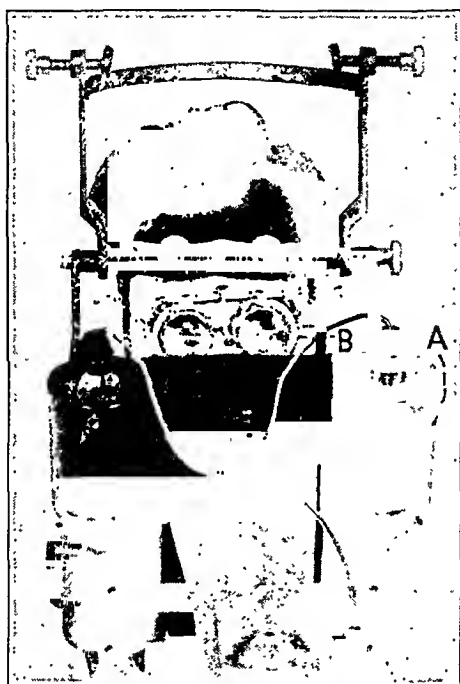
Fig. 2.—Photograph showing the position of the patient, the supplementary lights *A* and the half eye test lenses *B*.

The term "normal excursion" as used herein is not the average excursion of a number of normal eyes but is the excursion which any particular eye would make when reading lenses were not used.

Reference to figure 3 will serve to explain the manner in which a reading lens causes a greater or less excursion of the eye than normal. In each diagram *L* and *R* denote the left and right ends of a reading line; *P* and *F*, the points of a primary and final fixation in reading the line, and *VP* and *VF*, the points at which the visual axis meets the line when the eye is fixing *P* or *F*; the line *A—A*, drawn from the center of the reading line through *O* to the retina, is in each diagram both the visual axis and what may be termed the "fixation" axis when the eye is looking directly forward and is likewise the axis of the reading lenses shown in

figure 3 a and b. The point within the eye which has been termed the "visual center" as the visual axis always passes through it in any horizontal excursion of the eye is indicated by O.

Figure 3 a shows the excursion of an emmetropic eye when a reading lens is not used. When the eye is fixing P, as drawn, the visual and fixation axes coincide, and the fixation axis meets the reading line at
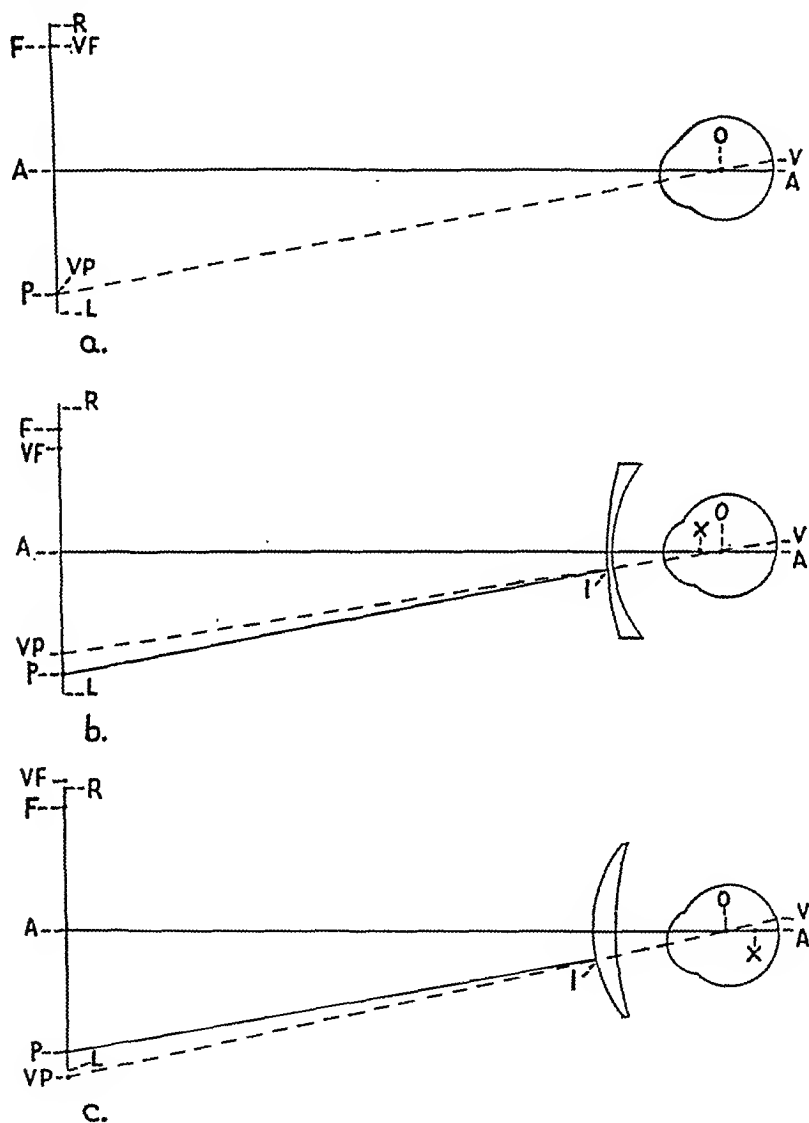
Fig. 3.—Diagrams showing the positions at which the visual axis is directed to meet the reading line when the eye is fixing P. The position for the emmetropic eye is shown in a; for the myopic eye, in b, and for the hyperopic eye, in c.

P, while the visual axis extends from the fovea at V, through O, to VP at the reading line, which is identical with P. In this same manner both the fixation and the visual axes meet the reading line at F and VF (which are identical) when the eye is fixing F. The normal excursion of the eye is then the "fixation" excursion from P to F, and when the visual

excursion VP to VF is identical thereto the graph will be a true record of the excursion of the eye from P to F.

In figure 3 b the excursion of a myopic eye is shown when a minus reading lens is used. When the eye is fixing P, as drawn, both the fixation and the visual axes coincide from the fovea at V, through O, to 1 at the reading lens, from which they diverge toward the reading line. As the center of the lens lies on A—A, the lens at 1 constitutes a spheroprism by decentration, the power of the prism element being dependent on the amount of the decentration and the dioptric power of the lens.

Thus when the eye is fixing P, the fixation axis from P to 1 is computed to locate 1 at such distance from the center of the lens on A—A that a continuation of P—1 would meet A—A at X; but it is deviated by the prism power of the lens at 1 to pass through O, and the visual axis from V to 1 will, if continued, meet the reading line at VP, and the distance from P to VP is computed. This same explanation serves when the eye fixes F, when 1 lies at the opposite side of A—A and the position of VF is determined. It is now evident that the effect of the reading lens is such as to permit a normal fixation excursion from P to F with a lesser excursion of the visual axis from VP to VF. As the excursion of the eye is recorded on the graph by light reflected from the cornea above and uninfluenced by the reading lens, the multiplication of the graphically recorded excursion by a factor greater than unity to convert it to normal, P to F, is obvious.

In figure 3 c the excursion of a hyperopic eye is shown when a plus reading lens is used. What has been said in relation to figure 3 b applies here as well, except that the deviation by the lens is in an opposite direction from that in figure 3 b and the computation of the distance of 1 from A—A is such that the fixation axis P—1 would, if continued, meet A—A at X but is deviated by the prism power of the lens to pass through O. The position of VP is at the opposite side of P, as is VF with reference to F, and the effect of the reading lens is such that a greater excursion of the eye, VP to VF, is necessary to permit the normal fixation excursion from P to F, and the multiplication of the recorded excursion by a factor less than unity is clearly indicated.

The tabulation and drawings serve to illustrate the effect of a lens on the excursion of the eye. This is pure mathematics and serves to explain the excursion of the eye as a man-made optical instrument.

The use of half-shaped reading lenses and, when necessary, of computation thus makes possible the determination of the excursion of any one eye in its relation to others in terms of the normal excursion of each eye, irrespective of whether or not reading lenses were used.

As a matter of interest, the factors pertaining to an abridged series of reading lens powers are given in the accompanying tabulation. The

first and third columns are the dioptric powers of a series of plus and minus reading lenses and at the right of each is the factor pertaining thereto.

Plus		Minus	
2.50	0.929	2.50	1.066
5.00	0.853	5.00	1.131
7.50	0.772	7.50	1.196
10.00	0.687	10.00	1.261
12.50	0.594	12.50	1.328
15.00	0.495	15.00	1.393

Four types of eyes were photographed: emmetropic, hyperopic, myopic and aphakic.

Figure 4 *A* and *B* shows photographs of the excursions of two emmetropic eyes while reading. Many ophthalmograms of this type were made.

Figure 4 *C* and *D* illustrate the photographic films of the excursions of two hyperopic eyes while reading through + 11 and + 13 lenses, respectively. The excursions of the eyes of 7 hyperopic patients were photographed, and all show this characteristic.

Figure 4 *E* and *F* shows photographs of the excursions of two myopic eyes reading through a — 13 lens. The excursions of the eyes of several myopic subjects were photographed, with similar results, as shown.

Figure 4 *G* and *H* shows the photographs of the excursions of two aphakic eyes reading through a + 13 lens. Twelve ophthalmograms of patients with aphakic eyes were made, with similar characteristics, as shown.

Since we were primarily interested in the excursion of the eyes in reading a line which is equal to the return excursion for reading the next line, this return excursion is used as being most convenient for measurements as illustrated.

We did not consider any other of the various points in the photographs, such as the time required for reading, the period for each fixation, the number of fixations or the number of regressions.

It will be noted that the excursions of emmetropic and hyperopic eyes, as demonstrated by the reading graphs, average from 6.5 to 7 mm., while those of aphakic eyes under similar circumstances are increased even to 10.5 or 11 mm. The myopic eyes move approximately 5 to 5.5 mm.

Ordinarily, when a photograph is made of an existing condition it is considered as accurate unless some artefact enters into the process
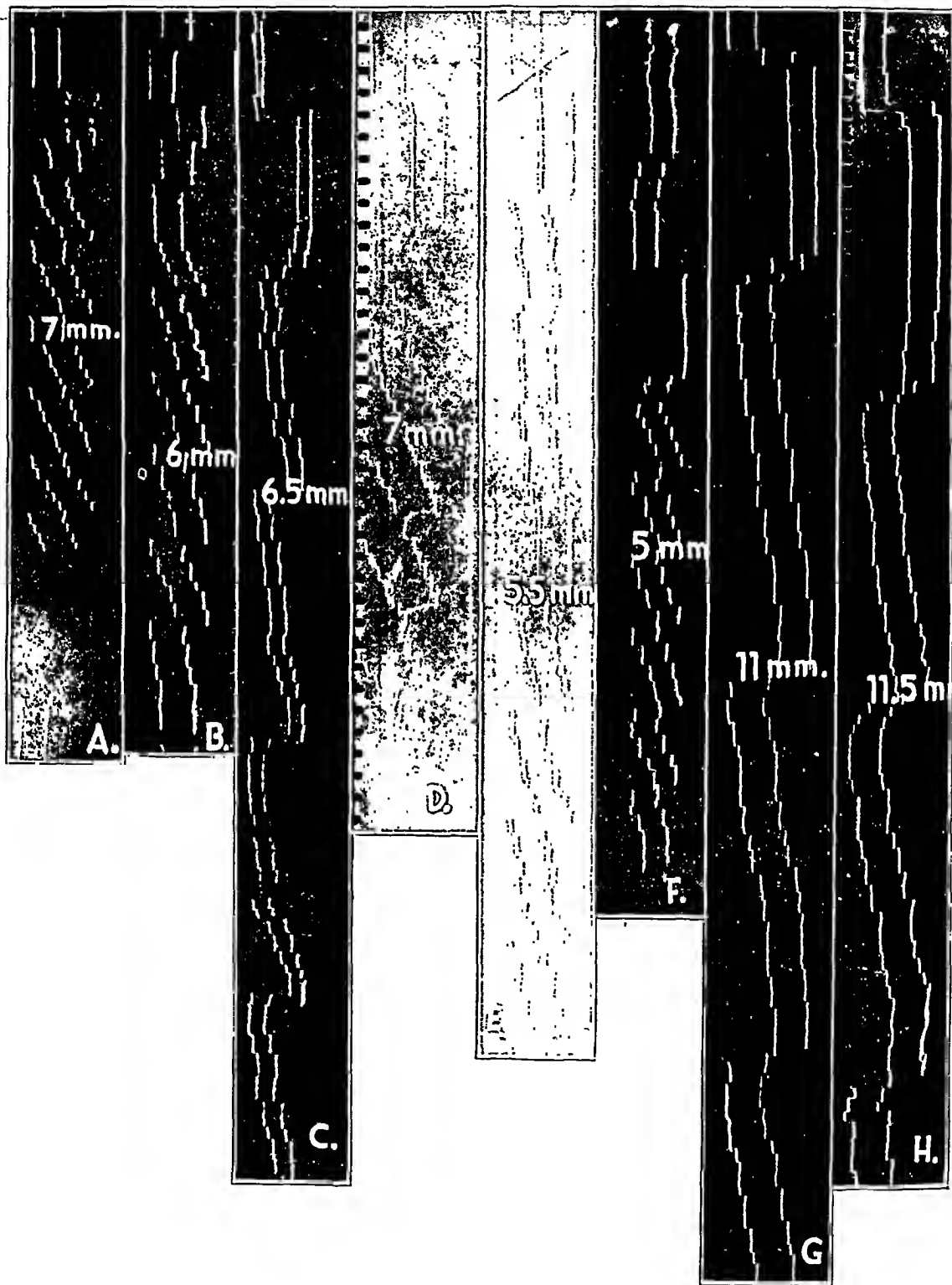
Fig. 4.—*A* and *B*, reading graphs of two emmetropic eyes; *C* and *D*, reading graphs of two hypcropic eyes while reading through + 11.00 and + 13.00 diopter lenses, respectively; *E* and *F*, reading graphs of two myopic eyes, while reading through — 13.00 diopter lenses in each case, and *G* and *H*, reading graphs of two aphakic eyes, each reading through a + 13.00 diopter lens.

of photographing. We have attempted to eliminate all possibilities of artefacts in this work; therefore, we feel that these reading graphs represent the actual situations. This eliminates the possibilities of erroneous personal observations, thus leaving the source of error only in their interpretation should there be an error committed.

The primary stimulus for central fixation is either a purposeful desire or a protective reflex action. In order to accomplish the purpose, the fovea must be brought to a position where the image of the object on which fixation is desired is brought by the visual axis to a focus on the fovea. When the desire for central fixation has been accomplished, the subject tested senses a feeling of introspective satisfaction, of achievement, irrespective of which combination or combinations of the aforementioned factors are present. Also, when this act has been completed the feeling of having accomplished the desire is of the same magnitude, irrespective of the physical status of the peripheral mechanism.

Since the visual axis is purely an imaginary beam of light, no one is able to locate accurately the position of the visual axis and its relation to the eyeball except with a specially constructed instrument and during stationary fixation. Therefore, any interpretation of reading graphs should be made with certain reservations in explaining the process of reading or seeing.

Many difficulties were encountered in completing this work. It is easy to photograph the reflexes from an eye with standard lighting, but as soon as the new system of lights were brought into use from above the reading material, the upper eyelids would interfere with the reflection. Not only that, but as soon as the patient consciously attempted to raise the eyelids, the eyeballs would advance, thereby blurring the light, which had previously been focused on the ground glass. Also, it was no easy task to find persons with high hyperopia who were old enough to concentrate while we were focusing the light on the ground glass as well as to be able to maintain fusion while reading.

Now that we recognize modificability in the mechanism of the eye, such as rotation with translation as well as the relation of positioning the eyeball for fixation, we should not attempt to formulate a theory according to any definite geometric diagram for monocular and binocular vision.

With these variable features to deal with, it would be unreasonable to assume that the relation of associated movements of convergence and accommodation, of divergence and relaxation of accommodation, of rotation and translation or of the rotation of the eyeball to a definite angular degree to move the visual axis for fixation should be considered as definitely fixed. Thus the main function of the visual mechanism would seem to be an integration of these associated movements, which vary

among themselves according to the stimuli which exist at any particular time and influence the sensorimotor system of the whole visual process. The visual process is complex and is affected not only by the physical state of the peripheral optic mechanism but also by the central perceptual and conceptual mechanism concerned in fixation and reading, which may in turn affect the peripheral optic mechanism through the autonomic as well as the skeletal nervous system. The mechanisms concerned in purposeful reading are only relatively steady or fixed in the homeostatic sense. The degree of their stability depends on the relative degree of normality of all the diverse activities which are synthesized into the whole conscious visual process.

CONCLUSIONS AND SUMMARY

We assume that the image of the point observed falls on the fovea.

The aphakic eye has removed the possibility of the lens and ciliary muscles influencing the position of the eye.

In reading a line the aphakic eye has to compensate for the reading lens, thereby causing a greater excursion.

The hyperopic eye, still maintaining its ciliary muscles and lens, is able to compensate for the reading lens so that the rectus muscles do not have to move the eye any further than an emmetropic eye.

A myopic eye still is able to compensate for the reading lens, so that the rectus muscles do not have to move the eyes as far as an emmetropic eye, thereby conserving much nervous and muscular energy as compared with the aphakic eye.

The autonomic nervous system not only controls the size of the pupil and the curvature of the lens but also plays a role in fixation. This role of the autonomic nervous system must be considered in a study of the causation and treatment of abnormalities of ocular functions.

The visual mechanism is not to be considered as fixed in a mathematical sense; it is only relatively fixed, as are all other physiologic processes in the body. Like other physiologic processes which are only relatively fixed, the visual mechanism is adaptable within limits and accordingly adapts itself to the physiologic and psychologic needs or contingencies or stimuli that exist at any particular moment. The concept of homeostasis [12] applies to visual processes as well as to other physiologic processes. The so-called laws pertaining to physiologic optics are only relatively true.

Mr. Clile C. Allen aided in the construction of the supplementary portion of the instrument used for this study.

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12. Cannon, W. B.: The Wisdom of the Body, ed. 2, New York, W. W. Norton & Company, Inc., 1939.

HYPERTROPHY OF THE THYMUS IN VERNAL CONJUNCTIVITIS

GUSTAVO ALAMILLA, M.D.

HABANA, CUBA

SYMPTOMATOLOGY

Literature relative to vernal conjunctivitis presents several points about this interesting disease which have greatly attracted my attention.

It is common knowledge that the condition manifests itself in children and is seldom found in persons over 20; that its periods of exacerbation begin in the spring; that it is characterized by photophobia, itching and slight catarrhal manifestations, and that it affects both the tarsal conjunctivas and the corneoscleral limbus. The tarsal conjunctiva begins to turn whitish, and in some cases floor tile–shaped or mosaic-shaped granulations are formed. In other cases the corneoscleral limbus becomes thicker, especially that part corresponding to the palpebral fissure. These clinical manifestations may appear either isolated or jointly; in the latter case the mixed form of vernal conjunctivitis is present. A great number of eosinophils are found in the scant secretion of the conjunctivas, and tests of the blood also show an increase in eosinophils.

The alterations caused by the disease become acute in the summer, diminishing during cold weather. This does not occur in every case, and the periods of exacerbation are not so noticeable in tropical countries as in those in which the difference in temperature between seasons is greater. At any rate, the disease shows notable remissions, and in some instances patients are temporarily relieved of all annoyance. Naturally, if the patient is thoroughly examined it will be observed that even in the cold months the manifestations do not entirely vanish but that alterations continue, although subjective symptoms may disappear altogether.

The exact causation of the disease is unknown. Lagrange and Delthil[1] in a monograph published in 1932 and Lagrange[2] in one published in 1935 stated that they considered vernal conjunctivitis to be an allergic disease of the pseudofollicular type. They pointed out the

From the Department of Ophthalmology, University of Habana.

1. Lagrange, H., and Delthil, S.: Les conjonctivites de nature anaphylactique, Paris, Gaston Doin, 1932.

2. Lagrange, H.: Le rôle de l'allergie dans certaines conjonctivites, Bull. Soc. d'opht. de Paris, April 1935, p. 231.

frequent association of this disease with endocrine disorders, alterations in the oculocardiac reflex and an imbalance of the vagosympathetic system and described certain startling results obtained with the administration of various endocrine preparations.

Woods [3] in 1937 showed his inclination to accept the inclusion of vernal catarrh as an allergic disease and stated as one of the conclusions of his paper on allergy, conjunctivitis and iritis that the present evidence indicates that vernal catarrh is an allergic disturbance.

Lehrfeld and Miller [4] in 1939 also reported that they favored the theory that the disease was of an allergic nature, but they stress the importance of the hereditary factor and suggested a relation to other atopic diseases.

These conclusions and the exhaustive research on which they are based certainly offer a definite stand in this important matter, but they cannot be considered as final until the cause of the disease is ascertained.

All that is positively known is that these manifestations succeed each other periodically and that they generally disappear when the patient reaches puberty, though in some instances they persist.

As to the treatment, nothing has been found up to the present to modify this condition substantially, although its annoyances can be relieved with the classic treatment of protecting the eyes with smoked lenses and applying astringent medications and in cases of extreme involvement, with local therapy and radium treatment.

ORIGIN OF AUTHOR'S INVESTIGATION

About four months previous to the writing of this report, I examined a 6 year old boy, T. S., who had acute vernal conjunctivitis of the mixed type, intense itching and abundant granulations. He was given the classic treatment, and the child's mother was warned of the periodicity of the condition, of which she was aware, as it was not the first time the boy had suffered from these symptoms. It was not until two months later that he returned to me with a foreign body in his cornea, and I was amazed to discover that both tarsal and sclerocorneal manifestations had disappeared, the boy appearing normal as far as his clinical aspect was concerned, free from any subjective sign, despite the fact that it was in the summer when, according to his mother, his condition always became worse.

I asked the mother whether the boy had received any other treatment outside of the hospital, and on her negative reply I verified from

3. Woods, A. C.: The Clinical Problem of Allergy in Relation to Conjunctivitis and Iritis, Arch. Ophth. **17**:1 (Jan.) 1937.

4. Lehrfeld, L., and Miller, J.: Additional Research on Vernal Conjunctivitis, Arch. Ophth. **21**:639 (April) 1939.

the clinical record that he had received only a series of intense irradiations of the thymus because of a diagnosis of extreme hypertrophy of this gland. A new blood test was made. At the previous visit eosinophilia was demonstrated, the eosinophil count being 14 per cent; at the later visit, the count was 4 per cent, which is within average limits. I wish to call attention to the fact that it was verified that this boy did not suffer from intestinal parasitism, which might have caused an increase in the number of eosinophils.

In an effort to find a cause for this unforeseen improvement, which surprised me greatly, I thought of a possible relation to the hypertrophy of the thymus, bearing in mind, in the first place, the fact that the patient showed considerable improvement after having received irradiation of the thymus but no other treatment; in the second place, the aforesaid well known fact that the symptoms of vernal conjunctivitis begin to decrease in pubescence, which is likewise the time at which the thymus undergoes a physiologic involution, and, in the third place, the facts that the association of this disease with endocrine disorders had been frequently found, as described by Lagrange and Delthil, and that numerous endocrine disorders were caused, in Pende's [5] opinion, by hypertrophy of the thymus and receded when this gland was subject to therapy. I decided to ascertain, therefore, whether all other patients with vernal conjunctivitis whom I had under treatment also had plain hypertrophy of the thymus, and in the event that this proved true I intended to find out whether the symptoms of vernal conjunctivitis would recede on irradiation of the thymus in each case.

VISUALIZATION OF THE THYMUS

Until Dr. Agustin Castellanos and Dr. Raul Pereiras, a pediatrician and a radiologist, respectively, both of the staff of the Children's Municipal Hospital of Habana, conceived a new technic for visualizing the thymus roentgenographically,[6] the diagnosis of hypertrophy of the thymus was made clinically, but no exact or reliable results were obtained therefrom.

Since with the average roentgen technic the thymus can seldom be visualized and then only in cases of extreme hypertrophy, I wish to describe the specialized technic of Dr. Castellanos and Dr. Pereiras, which consists of a simplification of the technic of anterior pneumo-

5. Pende, N.: Lezioni di patologia medica, Rome, Libraria Castellani, 1936.

6. Castellanos, A., and Pereiras, R.: El neumo-mediastino anterior: Un metodo nuevo para el diagnóstico de las hipertrofias del timo en la infancia, Arch. Soc. estud. clin., Habana **32**:97 (Oct.-Nov.) 1938; Superioridad del neumo mediastino en el diagnóstico de las formas atípicas de la hipertrofia del timo, Arch. de med. inf. **7**:327 (July-Sept.) 1938.

mediastinum formerly described by Cordorelli. This technic is, in my judgment, the pathognomonic means of making a diagnosis roentgenographically of an abnormal thymus gland.

Description of the Technic.—The instruments used consist of a 4 cm. hypodermic needle, bent until an angle of approximately 120 degrees is reached, so as to deviate the point 3 or 4 cm. off its base; a 50 cc. syringe with a thick good quality piston; a strong rubber hose 10 or 15 cm. long, with an interior diameter narrow enough to fit the syringe securely on one end and the needle on the other, and Péan tweezers.

The patient is placed in a supine posture with the head well stretched backward. The operator places himself behind the head of the patient. After antisepsis of the skin, the sternal notch is marked with the forefinger, and the curved needle is thrust in the middle. While the needle advances it will be made to describe a complete semicircle, going beyond the upper edge of the notch, until it is noted that it has touched the manubrium. Even if blood does not spurt spontaneously from the needle, the latter should be connected to the syringe and aspirations made to ascertain whether it has struck a large or small blood vessel. Blood seldom comes out, but in the event this should happen the needle should be pulled out and the operation performed again.

If it is found that no blood comes out, one end of the rubber hose is attached to the needle, the syringe is filled with air and adapted to the other end of the hose, and the air is slowly injected. Every time the syringe is emptied, the rubber hose is plugged with the Péan tweezers and the syringe recharged until the necessary amount of air is injected, which is controlled by fluoroscopic examination.

According to the authors, the amount of air to be injected varies from 40 to 150 cc. for children; as for adults, larger amounts can be safely injected. In a few cases as much as 500 cc. has been injected.

Often it happens that when a certain amount of air has been introduced, the patient feels a sensation of retrosternal pain, which is never intense. In such an event, the insufflation is discontinued for a few minutes or is maintained at a lower pressure. The time for reabsorbing the gas varies, but generally it has completely vanished after the third day.

With the anteroposterior posture, when the gaseous insufflation has been correct, a light shadow can be seen in the roentgenogram, 0.5 to 1 cm. thick, which encompasses the cardiac shadow and is even lighter around the vascular bundle. Almost every time the mediastinal pleura is made evident by the gas it is seen as a more or less undetermined zone, limiting on the outside the shadow of the injected gas. In order that this transparent zone may be shown more clearly, it is often necessary to tip the patient slightly in order to give the zone line a little slant.

The lateral posture generally gives a better view than the anteroposterior in cases in which the thymus is normal. A highly transparent zone is noted from the sternal notch to the diaphragm, its area, or rather its depth, depending greatly on the amount of air injected. No part of the pericardial sac or of the vascular bundle should join the back side of the sternum, and likewise no conduit or band of any sort whatever should exist between the mediastinal structures and the sternal zone.

When the thymus is normal, it is difficult to locate on account of its small size. Generally it is necessary to seek, under fluoroscopic control, the location wherein it is visualized, and many times it is necessary to place the patient in a

slanted or semislanted posture, since with the anteroposterior and the antero-lateral position usually used it cannot be visualized.

The thymus appears, viewed from the side, like an elongated narrow tongue, very flattened, high up and of high density and extremely small.

Roentgenograms should be taken from both sides, anterior and lateral, since only then can both portions of the mediastinum be viewed and the mediastinal shadows correctly interpreted, and also in a vertical position and during the inspiratory act.

Anterior pneumomediastinum has shown that many times the thymus is located behind the sternum, its two lobes forming columns or thick ropes longitudinally placed within the hili of the lungs. In this way the mediastinum appears of average width in roentgenograms taken by a normal procedure with the patient in an anteroposterior posture. This is the form Pereiras and Castellanos call "vascular" and is observed more frequently than is generally believed.

Furthermore, pneumomediastinum has shown that there exist many pathologic thymuses which produce atypical and bizarre roentgen shadows, which before this method was known gave rise to erroneous diagnoses, such as tracheo-bronchial adenopathy, perihilar infiltrations or shadows of the thick vessels.

PATHOLOGIC CHANGES IN .THE THYMUS

The dimensions of the thymus which can be considered as pathologic before puberty have been and still are the subject of much discussion.

Pende, as well as Hammar, considered that the persistence of thymus tissues after the age of 15 can be regarded as pathologic. This opinion, therefore, confirms the thesis generally accepted that the thymus undergoes physiologic involution when the average person reaches puberty. It is now admitted that some symptoms may be due to an increase in the size of the gland, which results in mechanical compressions, while others are the result of changes in the structure of the gland.

Anterior pneumomediastinum, by the method of Pereira and Castellanos, radiotherapy and the study of the clinical evolution of patients under observation have disclosed that a slightly hypertrophied thymus may cause the same intense, rebellious or grave symptoms as are produced by a highly hypertrophied thymus. This seems to indicate that the substances produced by the thymus, regardless of its size, are capable of affecting other glands, the vagosympathetic system and other parts and systems of the organism.

Only by an orderly and continued study of the greatest possible number of cases and roentgenograms in which the thymus appears visualized will it be possible to obtain positive answers to these important questions. To this end I have submitted a number of case reports with accompanying roentgenograms.

FIRST RESULTS OF AUTHOR'S INVESTIGATION

At the time I began my investigations there were 5 persons with vernal conjunctivitis in the ophthalmic service at the Calixto Garcia Hospital (University of Habana) and the dispensary of the Children's Municipal Hospital.

The patients ranged from 6 to 22 years of age.

After roentgenographic examination was made according to described technic, the children were all reported to show conspicuous hypertrophy of the thymus and the patients already in the pubescense, persistence and hypertrophy of the thymus, as may be verified in roentgenograms presented here.

As a measure of safety, I secured roentgenograms of the thymus of a number of children of the same age who clinically did not show symptoms of involvement of the thymus, and these proved that the size of the thymus of all these children was, in the respective ages, notably smaller than that of the children who showed symptoms of vernal conjunctivitis.

SPECIFICATIONS FOR THE IRRADIATION OF THE THYMUS IN CASES OF VERNAL CONJUNCTIVITIS

For patients actually in the pubescense or older, a dose of 30 roentgens per minute should be applied to an area of the thymus 10 by 15 cm. in size at a distance of 50 cm., 200 kilovolts, 15 milliamperes and filters of 1 mm. aluminum and 1 mm. copper being used. The total dose should be 800 roentgens, 200 being given each week.

For the treatment of patients who have not reached puberty, 40 roentgens per minute should be applied to an area of the thymus 10 by 15 cm. in size at a distance of 50 cm., 200 kilovolts, 15 milliamperes and filters of 1 mm. aluminum and 0.5 mm. copper being used. The total dose should be 400 roentgens at the rate of 100 roentgens weekly.

These doses, which can be considered as intermediate, should be augmented in those cases in which roentgen examination shows a persistence of hypertrophy of the thymus after their application.

REPORT OF CASES

CASE 1.—T. S., white, aged 6 years, was treated at the Children's Municipal Hospital. His tarsal conjunctivas showed some floor-tile-shaped granulations and a prominent corneoscleral ring. His blood showed 14 per cent eosinophils. The use of smoked lenses, closed on the sides, and astringents was prescribed as a local treatment. Intense irradiation was given, as the boy presented signs of mediastinal compression. He was seen again two months after the first examination. This time he had a foreign body in the cornea, which was removed, and the clinical signs and subjective symptoms of vernal conjunctivitis had disappeared, even though this was the period when his disease always became exacerbated.

CASE 2.—B. H., white, aged 6 years, was treated in the Children's Municipal Hospital on May 25, 1939. Both conjunctivas showed thick floor-tile-shaped granulations and a prominent ring in the sclerocorneal limb, and there was slight photophobia and intense itching of the eyes. The blood test showed an eosinophil count of 15 per cent. Roentgen examination of the thymus was made, and
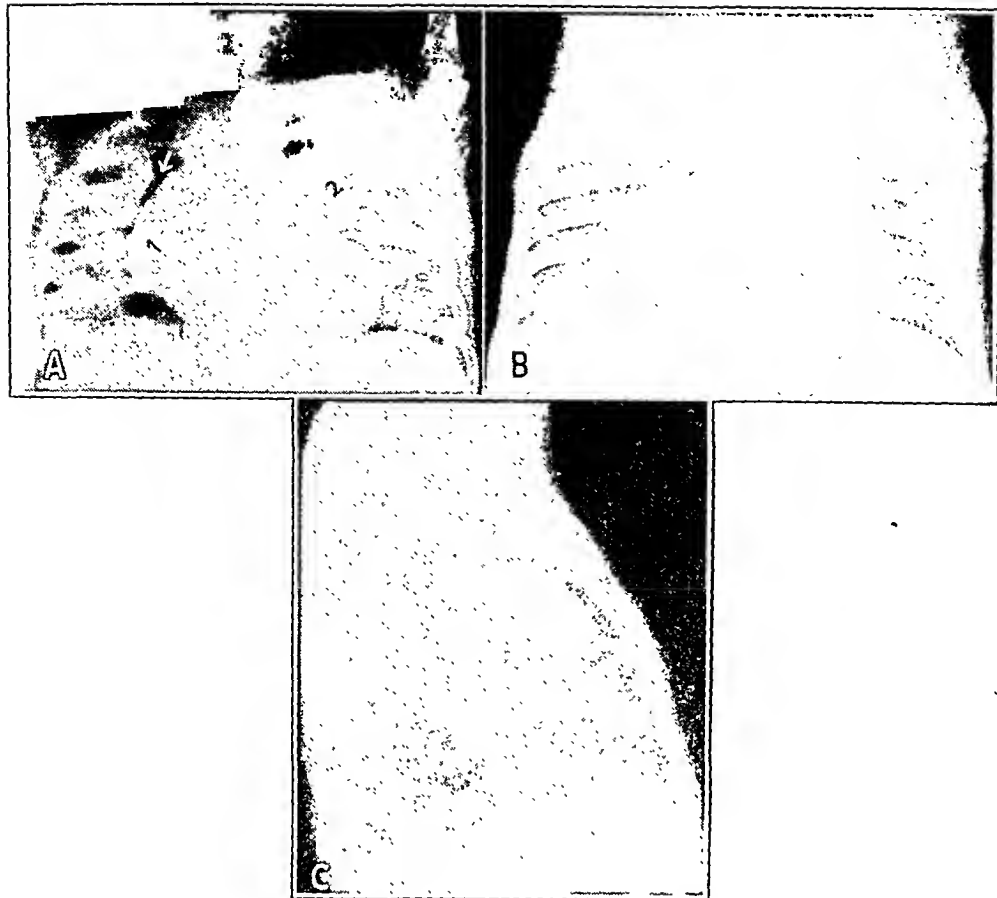
Fig. 1 (case 1).—*A,* roentgenogram made after anterior pneumomediastinum. The cardiac shadow as well as hypertrophy of both thymic lobules, whose contours are well marked by air, is quite noticeable. *B,* simple roentgenogram. The diagnosis made on the basis of this picture was mediastinal widening, probable ganglionic hypertrophy of the hili. *C,* lateral view made after anterior pneumomediastinum. The cardiac shadow as well as hypertrophy of both thymic lobules, whose contours are well marked by air, is quite noticeable.
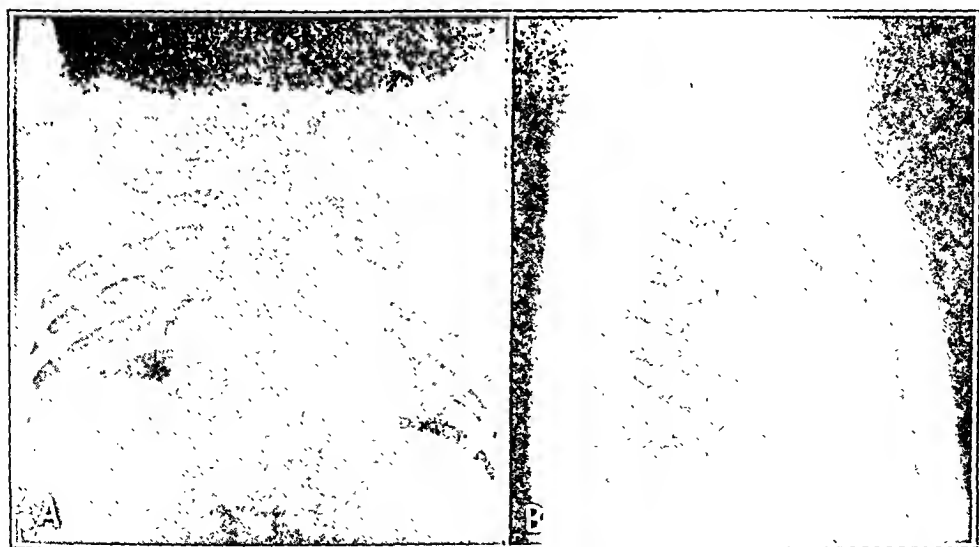
Fig. 2 (case 2).—*A,* anteroposterior roentgenogram showing the two thymic lobules made visible by pneumomediastinum. *B,* lateral view.

great hypertrophy was detected. The child was subjected to treatment, with the doses prescribed for children. On examination a month after completion of the treatment, there was considerable decrease in the granulations in both conjunctivas, especially on the right side, where they had almost disappeared. According to the girl's father, the itching and the sclerocorneal ring disappeared after the second application.

CASE 3.—M. P., white, aged 5 years, was examined on June 8, 1939, in the ophthalmic service of Calixto Garcia Hospital (University of Habana). A voluminous sclerocorneal ring was present, but there were no tarsal granulations. According to the mother, this was the first time the child had suffered from this condition. Her blood test showed an eosinophil count of 11 per cent, but a test of the secretion could not be made due to the restless state of the child. Pneumomediastinum was carried out, and hypertrophy of the thymus was demonstrated.

Fig. 3 (case 3).—Lateral view after pneumomediastinum showing great hypertrophy of the thymus.

The child was subjected to the treatment at the Cancer Institute with the dose prescribed for children. On examination before the end of the last application it was discovered that the itching sensation had disappeared and that the sclerocorneal ring had decreased in volume, although it was still clearly visible. An eosinophilia count of 9 per cent was demonstrated on the second test.

CASE 4.—O. H., white, aged 16 years, was treated in the ophthalmic service of the Calixto Garcia Hospital on June 12, 1939. Examination showed a pronounced thickening of the sclerocorneal limbus, with a whitish color. He stated that this was not the first year he had suffered from this condition, adding that he had had it since he was a small child and that this was one of the times it was more intense than usual. The palpebral conjunctivas were pale but did not show any granulations. There was intense itching but scanty secretion, which was mostly lacrimation. A test of the secretion showed a great amount of eosinophils, and a test of the blood gave an eosinophil count of 11 per cent. The patient
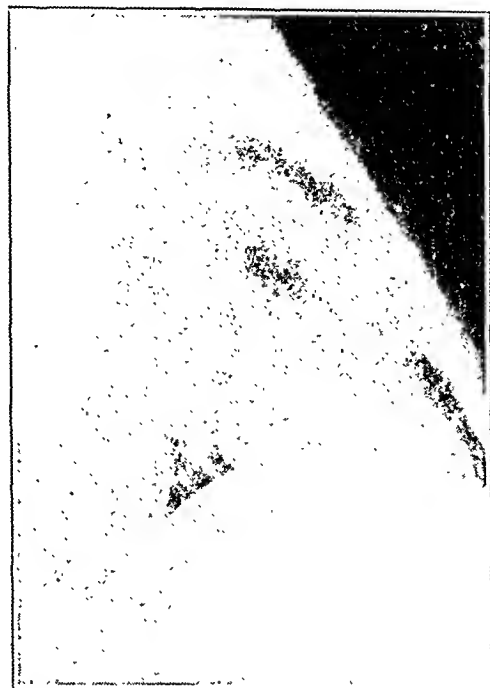
Fig. 4 (case 4).—Lateral view after pneumomediastinum showing a large thymic mass.

Fig. 5 (case 5).—Lateral view after pneumomediastinum showing great hypertrophy of the thymus.

was considered as an adult from the point of view of the thymus, and he received treatment for one month with the doses prescribed for an adult. He was again examined on July 21. No traces of the disease were found in the sclerocorneal limbus, and there were no subjective signs. He could not report for a new blood test as recommended because he had to leave town on short notice.

CASE 5.—L. G., a mulatto, aged 22, was seen in the ophthalmic service of the Calixto Garcia Hospital (University of Habana) on June 12, 1939. There were extensive granulations on the conjunctivas, a hard and thickened eyelid and traces of scars from two operations performed due to a diagnosis of trachoma. The patient stated that after each operation the granulations appeared with the same intensity. He presented a typical limbic ring, and a test of the secretion showed a great number of eosinophils. A test of the blood revealed an eosinophil count of 14 per cent. Roentgenograms showed extensive hypertrophy of the thymus, which could be clearly seen in the lateral plate. The patient was given the dose of radiation prescribed for adults. He was seen on July 24, that is, two days after finishing with his treatment, and examination showed that the limbic ring had vanished and that the granulations were smaller. The itching sensation had disappeared with the second irradiation. The eosinophil count in this case reached only 8 per cent.

COMMENT AND CONCLUSIONS

Despite the fact that the number of treated patients is rather small and that the time elapsed after the treatment is too short to arrive at definite conclusions, the improvement of the vernal conjunctivitis of patients subjected to this treatment has been so remarkable and the results so uniformly favorable that I consider that I can offer the hypothesis that hypertrophy of the thymus in children and persistence with hypertrophy of the thymus in adolescents and adults is the cause, or at least one of the factors, in the production of vernal conjunctivitis.

I will continue with my experiments until I have a sufficient number of patients to allow me to arrive at or to establish definite conclusions in favor of or against the hypothesis I have presented in this paper.

The study I have made and am still making in connection with this possible etiologic factor of vernal conjunctivitis has opened up an unsuspected series of possibilities concerning the pathologic changes in the thymus.

The presence of eosinophilic cells in the stroma of the thymus gland; the existence of eosinophilia in many thymus syndromes; their relations with certain manifestations, as, for example, eczema, and the frequency with which said symptoms are associated with fever, lead me to believe that changes in this gland are apt to influence or to produce an allergic state.

In the light of this conception, it could be held that the pathologic thymus, whether greatly hypertrophied or not, is the cause of a special biologic state or a part of a morbid constitution, one of the expres-

sions of which would be the vernal conjunctivitis. Irradiation of the thymus or its subsequent atrophy would cause the disappearance of those organic conditions which cause the vernal conjunctivitis.

I concur in the opinion that vernal conjunctivitis is of an allergic nature, but if, as I expect, the causation of the disease can be finally ascribed to a pathologic thymus, it will clearly point to the possibility that a pathologic thymus may be found a cause, or at least a determining factor, in other allergic diseases. In such a case a similar line of investigation as the one followed by me in the case of vernal conjunctivitis should be started.

But these points, which are beyond the scope of this work—related to vernal conjunctivitis only—will be the subject of subsequent works, which I will make known once the results obtained justify it.

DISCUSSION

Dr. Mark Andrew Gildea: Have roentgenograms been taken to see if the thymus had decreased in size after treatment?

Dr. Gustavo Alamilla, Habana, Cuba: In answer to Dr. Gildea's question, I have had some roentgenograms taken after treatment in other cases of allergic manifestations but not in cases of vernal conjunctivitis. My report is a preliminary one, and my intention in presenting it is to give other colleagues the opportunity to find out if their observations coincide with mine.

Dr. Mark J. Schoenberg: May I ask how Dr. Alamilla explains (1) the cases of enlarged thymus without signs of vernal catarrh, (2) the exacerbation of symptoms in hot or moist weather and (3) the fact that infants, in whom the thymus is usually large, do not suffer from vernal catarrh?

Dr. Gustavo Alamilla, Habana, Cuba: These patients may not have symptoms of vernal catarrh, but they frequently have other symptoms of an allergic nature. As to the exacerbation during hot weather, this occurs only in animals.

Dr. David Wexler: Were there symptoms of respiratory difficulty due to tracheal compression in some of the cases of thymic enlargement?

Dr. Gustavo Alamilla, Habana, Cuba: Yes, there were not only respiratory symptoms but also symptoms due to endocrine disturbances, especially those associated with disturbances of the sexual glands. In the last case reported in my paper the patient presented not only vernal catarrh but also other endocrine changes. I have 1 case in which a diagnosis of asthma was made, but roentgen examination revealed hypertrophy of the thymus. Roentgen treatment of the gland brought about cure. The patient did not present vernal catarrh. The only symptom was asthma.

Dr. Murray Last: Are cases of status thymus lymphaticus included in this group—those cases in which there is enlargement of the thymus and hypoplasia of the heart and blood vessels?

Dr. Gustavo Alamilla, Habana, Cuba: I have had no experience with the cases mentioned by Dr. Last.

Dr. Daniel M. Rolett: I want to ask whether in the cases observed there were any other outstanding allergic manifestations except those already described and pertaining to vernal conjunctivitis.

Dr. Gustavo Alamilla, Habana, Cuba: There were other allergic symptoms besides vernal conjunctivitis, and for this reason I have not limited my study to cases of vernal catarrh. I am continuing my research and am studying cases of allergic manifestations.

EFFECTS OF SULFANILAMIDE AND SULFAPYRIDINE ON THE KOCH-WEEKS BACILLUS (HAEMOPHILUS INFLUENZAE)

JACK S. GUYTON, M.D.

BALTIMORE

The Koch-Weeks bacillus (Haemophilus influenzae) [1] is one of the most frequent causes of conjunctivitis. It is commonly regarded as a more or less benign organism, producing a self-limited contagious inflammation of the conjunctiva. However, it not infrequently produces corneal ulceration, severe purulent conjunctivitis or a persistent muco-purulent conjunctivitis. This organism is therefore of sufficient importance to justify an investigation of its susceptibility to sulfanilamide and sulfapyridine.

SUMMARY OF PREVIOUS LITERATURE

Long and Bliss [2] in 1937 found that sulfanilamide in a concentration of 10 mg. per hundred cubic centimeters inhibited the growth of the influenza bacillus in vitro. The organisms were grown in blood broth cultures, the inhibition of growth being determined by gross comparison with control cultures. [3] The strain of organism used was thought to be an encapsulated "mucoid" type a. [4]

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1. Various strains of the Koch-Weeks bacillus and the Pfeiffer influenza bacillus possess identical cultural, morphologic and serologic characteristics. The identity of these organisms was established by German investigators in the early 1920's (Knorr, M.: Das Koch-Weekssche Bacterium und der Pfeiffersche Influenzabacillus, Ergebn. d. Hyg., Bakt., Immunitätsforsch. u. exper. Therap. 6:350, 1924. Knorr, M., and Gehlen, W.: Untersuchungen über einen Erreger der ägyptischen Augentzündung [Koch-Weekssches Bakterium] und seine Beziehungen zum Pfefferschen Influenzabacillus; V. Das Wachtsum der hämophilen Keime in pflanzlichen Nährmitteln, Centralbl. f. Bakt. 95:295, 1925. Fincterwalder, C.: Untersuchungen über Koch-Weekssche Bazillen, Arch. f. Hyg. 100:5, 1928. Schmelzer, H., and Eckstein, E.: Ueber Koch-Weeks-Bacillen-Conjunctivitis, Arch. f. Ophth. 132:20, 1934) and is generally recognized by English-speaking bacteriologists; however, this identity appears to have been overlooked in both the English and the American ophthalmic literature.

2. Long, P. H., and Bliss, E. Z.: Para-Amino-Benzene-Sulfonamide and Its Derivatives: Experimental and Clinical Observations on Their Use in the Treatment of Beta-Hemolytic Streptococcic Infection, J. A. M. A. 108:32 (Jan. 2) 1937.

3. Long, P. H.: Personal communication to the author.

4. Pittman, M.: Type Specificity in Hemophilus Influenzae, J. Exper. Med. 53:488, 1931. Chandler, C. A.; Fothergill, L. D., and Dingle, J. H.: The Pattern of Dissociation in Hemophilus Influenzae, J. Bact. 37:415, 1939.

Povitsky,[5] using a strain of H. influenzae isolated from a patient with meningitis, investigated the protective effects of azosulfamide (neoprontosil; disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene 3',6'-disulfonate) and of anti-influenza serum on mice inoculated intraperitoneally. He found that no significant effect was exerted by either the neoprontosil alone or the serum alone. However, the mortality of the mice was lowered from 100 per cent among the controls to from 13 to 33 per cent among the test animals when both azosulfamide (neoprontosil) and serum were administered initially and were given again the same day and the next day. The type of serum used was not stated. The inoculum used for each mouse was two loops of a standardized culture, not suspended in mucin. This amount proved fatal to 100 per cent of the controls, but half this amount caused the death of only about 60 per cent of untreated mice.

Pittman[6] recently reported a case of purulent conjunctivitis, mastoiditis and pneumonia in which a nonencapsulated "smooth" strain of H. influenzae was the causative agent. The patient promptly recovered after the oral administration of sulfapyridine. Pittman found that the mucin virulence for mice of the organism recovered from this patient was excessively high, the minimal lethal dose being approximately 500 organisms. However, when sulfapyridine was introduced into the stomachs of mice one-half hour before intraperitoneal inoculations of 100 minimal lethal doses of this organism, a number of mice survived. The percentage of survival varied directly with the dose of sulfapyridine, being 70 to 100 per cent for the groups treated with the maximum dose (8 mg.). Only an initial dose of sulfapyridine was required for lasting protection. (A peculiar feature of infections in mice due to H. influenzae is the fact that all deaths occur during the first three days after inoculation, most of them during the first twenty-four hours, and that all mice surviving as long as three days recover completely.)

A number of patients with influenzal meningitis have been treated with sulfanilamide compounds. Recovery in isolated cases has been reported by Jones[7] after sulfanilamide therapy, by Folsom and Gerchow[8] after treatment with sulfanilamide and azosulfamide (neoprontosil) and by Teggart[9] after treatment with soluseptasine (disodium p-(γ-phenylpropylamino)-benzenesulfonamide-α-γ-disulfonate). Young

5. Povitsky, O. R.: Immune Serum and Prontosil: Combined Treatment for Protection of the Mouse Against Fatal Dose of Hemophilus Influenza Meningitis; Preliminary Report, New York State J. Med. **37**:1748, 1937.

6. Pittman, M.: Protection of Mice Against Hemophilus Influenzae Non-Type-Specific with Sulfapyridine, Pub. Health Rep. **54**:1769, 1939.

7. Jones, H. W. E.: H. Influenzae Meningitis, Brit. M. J. **2**:797, 1937.

8. Cited by Bigler, J. A., and Haralambie, J. Q.: Sulfanilamide and Related Compounds: A Review of the Literature, Am. J. Dis. Child. **57**:1110 (May) 1939.

9. Teggart, B.: Influenzal Meningitis Treated with Soluseptasine and Lumbar Puncture: Recovery, Brit. M. J. **1**:1365, 1938.

and Moore [10] reported the recovery of a patient treated with sulfanilamide and Fothergill's anti-influenza serum. Hamilton and Neff [11] reported a case in which the patient improved greatly during a five day course of treatment with sulfapyridine, had a relapse two days after stopping the administration of the drug, and recovered completely during a further fifteen day course of treatment with the drug. Neal [12] reported the recovery of only 2 of 18 patients treated with sulfanilamide, azosulfamide (neoprontosil) and anti-influenza serum. Five cases of this disease in which treatment with sulfanilamide was unsuccessful were reported in a symposium on sulfanilamide. [13] Taylor [14] treated a patient unsuccessfully with sulfanilamide, azosulfamide (neoprontosil) and immune serum. Appelbaum's [8] patient, treated with sulfanilamide, also died. Barnett and Hartmann [15] recorded 2 cases in which sulfapyridine therapy had no appreciable effect on the course of the disease.

The reports cited afford little evidence that sulfanilamide compounds exert a favorable influence on the course of influenzal meningitis. If one discards the reports of isolated recoveries as possible chance occurrences, the percentage of recovery of those patients receiving sulfanilamide compounds has been what would be expected without chemotherapy. However, the small number of patients treated and the widely varying doses used prevent any negative conclusions being drawn, and the possibilities of effective treatment with sulfapyridine or with sulfapyridine plus anti-influenza serum remain to be proved.

More favorable evidence of the beneficial effects of sulfanilamide on infections due to H. influenzae is afforded by Albright and his co-workers, [16] who reported 2 cases of nephrocalcinosis caused by per-

10. Young, R. H., and Moore, C.: Influenzal Meningitis: Report of a Case Treated with Anti-Influenzal Serum and Sulfanilamide, Arch. Pediat. 55:282, 1938.

11. Hamilton, T. R., and Neff, F. C.: Influenzal Meningitis with Bacteremia Treated with Sulfapyridine: Recovery, J. A. M. A. 113:1123 (Sept. 16) 1939.

12. Neal, J. B.: Treatment of Acute Infections of the Central Nervous System with Sulfanilamide, J. A. M. A. 111:1353 (Oct. 8) 1938.

13. Basman, J., and Parley, A. M.: Report of Patients Treated with Sulfanilamide at the St. Louis Children's Hospital, J. Pediat. 11:212, 1937. Hageman, P. O.: Clinical Experience in the Use of Sulfanilamide at the New Haven Hospital, ibid. 11:195, 1937. McQuarrie, Q.: Report of Cases Treated with Sulfanilamide (Prontosil and Prontylin), ibid. 11:188, 1937. McIntosh, R.; Wilcox, D. A., and Wright, F. H.: Results of Sulfanilamide Treatment at the Babies' Hospital, New York City, ibid. 11:167, 1937.

14. Taylor, H. W.: Treatment of a Case of Influenzal Meningitis with Immune Serum and Sulfanilamide, Arch. Pediat. 55:131, 1938.

15. Barnett, H. L.; Hartmann, A. F.; Perley, A. M., and Ruhoff, M. B.: The Treatment of Pneumococcic Infections in Infants and Children with Sulfapyridine, J. A. M. A. 112:518 (Feb. 11) 1939.

16. Albright, F.; Dienes, L., and Sulkowitch, H. W.: Pyelonephritis with Nephrocalcinosis Caused by Haemophilus Influenzae and Alleviated by Sulfanilamide: Report of Two Cases, J. A. M. A. 110:357 (Jan. 29) 1938.

sistent infections with H. influenzae. Administration of sulfanilamide resulted in prompt disappearance of the influenza bacillus from the urine and alleviation of symptoms in each patient. (A much higher concentration of sulfanilamide can be attained in the urine than in the blood of a patient.) There appears to be little doubt as to the therapeutic effect of sulfanilamide in both of these cases.

EXPERIMENTAL WORK

Experiments were undertaken to show the in vitro effects of various concentrations of sulfanilamide and sulfapyridine on the growth of H. influenzae.

Materials and Methods.—Strain KS was obtained from the conjunctival sac of the patient in case 3, reported in this paper. It is a nonencapsulated "smooth" strain, forming colonies on Fildes' medium [17] indistinguishable from the colonies of most respiratory strains.

Strain KM was obtained from Dr. Margaret Pittman, of the National Institute of Health in Washington. It is an encapsulated "mucoid" type b strain. (The large majority of cases of influenzal meningitis are caused by a type b strain.) It showed no tendency to dissociate while it was being used, forming only large, iridescent colonies on Fildes' medium.

Beef heart infusion broth containing 1 per cent neopeptone and 5 per cent defibrinated rabbit blood was employed as the culture medium. In order to produce an even culture, the strain being used was transplanted three separate times at twenty-four hour intervals before beginning each experiment. Serial dilutions of the last twenty-four hour culture were then made and an appropriate dilution selected for inoculation into tubes containing sulfanilamide or sulfapyridine. The number of bacterial units per cubic centimeter in the culture dilution selected for each experiment was determined by planting 0.5 cc. of various dilutions in blood agar pour plates and counting the resulting colonies.

Sets of three tubes each, containing various concentrations of sulfanilamide and sulfapyridine in 5 cc. of blood broth, were then inoculated with 0.5 cc. of the culture dilution decided on for that experiment. Control tubes containing no sulfanilamide or sulfapyridine were similarly inoculated. These tubes were all incubated at 37 C. for from eighteen to twenty-three hours. Serial dilutions from each of these tubes were then made in plain broth. Various of these dilutions were planted in 0.5 cc. quantities in blood agar pour plates. The number of bacterial units per cubic centimeter in each of the tubes incubated was calculated from a count of the resulting colonies in the pour plates.

Results.—The results of five experiments with regard to the effects of sulfanilamide and sulfapyridine on the growth of H. influenzae in blood broth are given in tables 1 and 2. Experiments A, B, C and D (table 1) portray effects of different concentrations of these drugs on the growth of strain KS. Experiments E and F (table 2) indicate

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17. Fildes, P.: A New Medium for the Growth of B. Influenzae, Brit. J. Exper. Path. **1**:129, 1920.

TABLE 1.—*Effects of Sulfanilamide and Sulfapyridine on the Growth of Strain KS (Smooth) H. Influenzae in Blood Broth*

Inoculum and Period of Incubation	Set	Tube	Drug Used and Concentration, Mg. per 100 Cc.	Growth (In Bacterial Units per Cc.)	Average Logarithm of Growth of Each Set ($\bar{x}$)†
A Inoculum, 5.5 Period of incubation, 23 hr.	1	a b c	Control............	126,000,000 119,000,000 93,000,000	8.0481
	2	a b c	Sulfanilamide 1......	30,400,000 34,000,000 24,000,000	7.4649
	3	a b c	Sulfanilamide 3.2....	3,200,000 1,800,000 9,800,000	6.5839
	4	a b c	Sulfapyridine 3.2.....	0* 0* 0*	
B Inoculum, 98 Period of incubation, 22 hr.	1	a b c	Control............	160,000,000 156,000,000 170,000,000	8.2092
	2	a b c	Sulfanilamide 3.2....	36,000,000 18,400,000 24,000,000	7.4004
	3	a b c	Sulfanilamide 10.....	640,000 1,280,000 1,090,000	5.9743
	4	a b c	Sulfapyridine 3.2.....	0* 0* 28,000	
	5	a b c	Sulfapyridine 10.....	0+ 0* 0*	
C Inoculum, 1,600 Period of incubation, 18 hr.	1	a b c	Control............	9,600,000 5,900,000 14,600,000	6.9725
	2	a b c	Sulfanilamide 10.....	7,400,000 14,000,000 8,600,000	6.9833
	3	a b c	Sulfanilamide 50	40,000 11,000 16,000	4.2825
	4	a b c	Sulfapyridine 10.....	3,500,000 3,600,000 1,200,000	6.3932
	5	a b c	Sulfapyridine 50.....	180,000 49,000 100,000	4.9818
D Inoculum, 4,000 Period of incubation, 23 hr.	1	a b c	Control............	80,000,000 166,000,000 256,000,000	8.1771
	2	a b c	Sulfanilamide 1......	176,000,000 152,000,000 192,000,000	8.2369
	3	a b c	Sulfanilamide 3.2....	72,000,000 59,000,000 147,000,000	7.9319
	4	a b c	Sulfapyridine 1......	30,400,000 32,000,000 33,000,000	7.5022

* There was also no growth from the original tube after seventy-two hours of incubation.

† The average logarithm of growth of each set is given to afford ready statistical comparison. A difference in the average logarithms of 2 sets of over 0.6022 may be considered statistically significant, i. e.: Relative counts of organisms are usually distributed somewhat like the normal curve. Relative values may be obtained by taking logarithms of the counts. On the assumption that the readings of each of the 23 sets portray the same relative error, one may estimate the common relative error of all sets by taking an appropriate average of the 23 standard deviations. Such an average is given by S $= \sqrt{\dfrac{S\ [\Sigma\ (x - \bar{x})^2]}{N}} = 0.2563$, in which x refers to an individual logarithm, $\bar{x}$ to the average of the 3 readings for that set, Σ to summation over the 3 values of the set, S to summation over the 23 sets and N to the total number of degrees of freedom available for making the estimate (in this case 46 since each set contributes 2). The difference in average logarithms of 2 sets with the same inoculum may then be compared with the estimated standard deviation of the difference, S$\sqrt{\tfrac{2}{3}}$, or 0.2033, and judgment as to significance made by reference to the normal curve. To be judged significant, a difference may be required which would be exceeded on the basis of chance alone less than 5 per cent of the time (in this case a difference greater than 0.4582) or, more conservatively, less than 1 per cent of the time (a difference greater than 0.6022).

similar effects noted on the growth of strain KM. An inoculum of different size was used in each experiment, the size of the inoculum as expressed in bacterial units being indicated in the tables.

TABLE 2.—*Effects of Sulfanilamide and Sulfapyridine on the Growth of Strain KM (Mucoid Type b) H. Influenzae in Blood Broth*

Inoculum and Period of Incubation	Set	Tube	Drug Used and Concentration, Mg. per 100 Cc.	Growth (in Bacterial Units per Cc.)			Average Logarithm of Growth of Each Set (x̄)†
E Inoculum, 7.5 Period of incubation, 23 hr.	1	a b c	Control.............	{	160,000,000 16,000,000 142,000,000	}	7.8335
	2	a b c	Sulfanilamide 1......	{	0* 0* 0*		
	3	a b c	Sulfanilamide 3.2....	{	0* 0* 0*		
	4	a b c	Sulfanilamide 10.....	{	0* 0* 0*		
	5	a b c	Sulfapyridine 1......	{	0* 0* 0*		
	6	a b c	Sulfapyridine 3.2.....	{	0* 0* 0*		
	7	a b c	Sulfapyridine 10.....	{	0* 0* 0*		
F Inoculum, 470 Period of incubation, 23 hr.	1	a b c	Control.............	{	304,000,000 246,000,000 320,000,000	}	8.4596
	2	a b c	Sulfanilamide 1......	{	200,000,000 226,000,000 156,000,000	}	8.2327
	3	a b c	Sulfanilamide 3.2....	{	124,000,000 62,000,000 70,000,000	}	7.9103
	4	a b c	Sulfanilamide 10.....	{	9,200,000 7,800,000 9,400,000	}	6.9430
	5	a b c	Sulfapyridine 1......	{	1,600,000 1,400,000 1,000,000	}	6.1167
	6	a b c	Sulfapyridine 3.2.....	}	3,000 9,000 3,000	}	3.6361
	7	a b c	Sulfapyridine 10.....	{	3,000 2,400 27,600	}	3.7661

* See footnote under table 1.
† See footnote under table 1.

Analysis of Results.—1. Both sulfanilamide and sulfapyridine exert a marked inhibitory effect on the growth of H. influenzae in blood broth. The quantitative effect noted varies in general directly with the concentration of the drug and inversely with the size of the inoculum (but not in a linear ratio). With small inoculums, both drugs may exert a bactericidal effect.

2. With inoculums of comparable size (experiments A and E), the growth of strain KM appears to have been inhibited more than that of strain KS.

3. In concentrations of 1 to 10 mg. per hundred cubic centimeters, sulfapyridine exerted a significantly greater effect than the corresponding concentration of sulfanilamide. On comparison of set F4 with set F5, it is noted that a significantly greater effect was produced by 1 mg. per hundred cubic centimeters sulfapyridine than by 10 mg. per hundred cubic centimeters sulfanilamide.

TABLE 3.—*Results of Oral Administration of Sulfanilamide or Sulfapyridine to Patients with Ocular Infections Due to H. Influenzae*

Case No.	Age, Yr.	Type of Infection	Drug Used	Average Blood Concentration, Mg. per 100 Cc.	Days of Therapy	Results
1	27	Acute purulent conjunctivitis in right eye of 4 hours' duration; pure culture of H. influenzae from right eye and from throat	Sulfanilamide	9	3	Markedly improved, with negative cultures, within 24 hr.; complete clinical cure within 3 days
2	28	Acute recurrent dacryocystitis; incision and drainage on 4th day; pure culture of H. influenzae from lacrimal sac; inflammation worse on 5th day; administration of sulfanilamide then started	Sulfanilamide	7	5	Discharge completely ceased within 2 days and swelling disappeared within 3 days; recurrence of dacryocystitis 9 days after stopping administration of sulfanilamide, with pure culture of H. influenzae obtained from conjunctival sac; inflammation began to subside 1 day after starting administration of sulfanilamide again; uneventful dacryocystectomy performed 2 days later
3	60	Severe hypopyon ulcer in right eye of 6 days' duration; H. influenzae, Staph. albus and diphtheroids grown from right eye	Sulfapyridine	7	21	Marked improvement within 48 hr.; staphylococci and diphtheroids only could be grown after 2 days; progressive healing of ulcer, complete within 18 days; final vision in left eye 20/70

4. With a large inoculum, sulfanilamide in a concentration of 50 mg. per hundred cubic centimeters produced a greater effect than did sulfapyridine in a concentration of 50 mg. per hundred cubic centimeters (sets C3 and C5). These concentrations were used in only 1 instance. (Differences greater than that observed arise as a result of chance alone only three times per thousand.) It is also notable that in one instance sulfapyridine in a concentration of 10 mg. per hundred cubic centimeters had no greater effect than the same drug in a concentration of 3.2 mg. (sets F6 and F7). These observations may indicate that the relative effectiveness of increasing the concentration of the drug is not as great for sulfapyridine as it is for sulfanilamide.

REPORT OF CASES

During the past six months 3 patients admitted to the Johns Hopkins Hospital have had ocular infections due to H. influenzae which were considered sufficiently severe to justify the oral administration of sulfanilamide or sulfapyridine. A summary of these cases is given in table 3. The response of each of these patients to chemotherapy appeared to be more rapid than could be accounted for on the basis of chance.

TABLE 4.—*Effects of Local Therapy with an Ointment Containing Sulfanilamide on Ocular Infections Due to H. Influenzae*

Case No.	Age, Yr.	Type of Infection	Initial Culture	Instillations of Sulfanilamide Ointment*	Instillations of Control Ointment†	Results
4	29	Moderate hypopyon ulcer of left eye of 12 days' duration; right eye not inflamed	Right eye: Staph. albus and diphtheroids; left eye: H. influenzae, Staph. albus and diphtheroids	To left eye every hour for 3 days; then instillations reduced to every 4 hours for 8 days	None	Ulcer slowly but progressively healed during 12 days' time: cultures at first showed light growth of same organisms found initially but H. influenzae could not be grown after 12th day
5	40	Bilateral recurrent conjunctivitis with superficial corneal ulceration; duration of present attack, 2 mo.	Right eye: H. Influenzae, Staph. albus and diphtheroids; left eye: H. influenzae, Staph. albus and diphtheroids	To right eye every hour while awake for 19 days	To the left eye every hour while awake for 19 days	Inflammation slowly subsided in both eyes but never completely disappeared during the period of treatment; repeated culture always grew the same organisms as the initial culture
6	3	Bilateral chronic mucopurulent conjunctivitis since birth	Right eye: H. influenzae and Staph. albus; left eye: H. influenzae and Staph. albus	To the right eye every hour while awake for 14 days	To the left eye every hour while awake for 19 days	Progressive clinical improvement of both eyes during the period of treatment; H. influenzae and Staph. albus grown from both eyes after 2 days but cultures from both eyes sterile thereafter

* The ointment used in case 4 consisted of 5 per cent sulfanilamide in a castor oil-petrolatum base and that used in cases 5 and 6 consisted of 5 per cent sulfanilamide in a water-soluble tragacanth-glycerin base.

† The control ointment used in the last 2 cases was a tragacanth-glycerin base without sulfanilamide.

Three patients with ocular infections due to H. influenzae less severe than those mentioned were treated with an ointment containing sulfanilamide. This method of treatment does not appear to have been efficacious. A summary of these cases is given in table 4. The ocular inflammation progressively subsided in all of these patients, but in cases 5 and 6 exactly the same effect was noted in the eyes which received a control ointment as in the eyes which received the ointment containing sulfanilamide.

SUMMARY

The previous literature on this subject is briefly reviewed. These reports indicate that sulfanilamide exerts an inhibitory effect on the in vitro growth of H. influenzae and that both sulfanilamide and sulfapyridine may at times have a beneficial in vivo action against certain types of infection due to this organism.

In vitro experiments with regard to the effects of these two drugs on the growth of two strains of H. influenza in blood broth cultures indicate:

(a) Both drugs may produce an inhibitory or a bactericidal effect.

(b) The growth of the encapsulated "mucoid" type b strain used appears to have been inhibited more than the growth of the nonencapsulated "smooth" strain.

(c) Sulfapyridine in concentrations used therapeutically (1 to 10 mg. per hundred cubic centimeters) exerts a much greater effect than does sulfanilamide in these concentrations.

(d) Conversely, in concentrations of 50 mg. per hundred cubic centimeters sulfanilamide appears to be more effective than sulfapyridine.

The oral administration of sulfanilamide to 2 patients and of sulfapyridine to 1 patient with ocular infections due to H. influenzae produced significant therapeutic effects.

The local treatment of 3 patients with ocular infections due to H. influenzae with an ointment containing 5 per cent sulfanilamide produced no significant beneficial effects.

GYRATE ATROPHY OF THE RETINA AND CHOROID FOLLOWING RETINITIS PIGMENTOSA

REPORT OF TWO CASES

WILLIAM THORNWALL DAVIS, M.D.

AND

ERNEST SHEPPARD, M.D.

WASHINGTON, D. C.

Gyrate atrophy of the retina and choroid was first described by Cutler [1] and Fuchs.[2] Nettleship [3] has exhaustively studied retinitis pigmentosa and allied conditions with particular reference to consanguinity and heredity. Because the symptomatology is similar, he included in his extensive study retinitis pigmentosa sine pigmento, retinitis punctata albescens (Mooren and Gayet), gyrate atrophy of the retina and the choroid (Fuchs), congenital stationary night blindness without changes and choroideremia. Other associated deficiencies which he found were deafness; deaf-mutism; various grades of mental deficiency, including idiocy and insanity; epilepsy, and progressive paralysis, apparently spinal but not thoroughly analyzed. Also observed were polydactylism, coloboma of the iris, remnants of the hyaloid artery, congenital cataract and posterior cortical cataract without other changes, conical cornea, a peculiar condition of the skin, heterochromia of the iris and color blindness.

Bedell [4] recently presented a thorough review of the literature of choroideremia, in which he stated: ". . . no two cases are alike in regard to the distribution of pigment, the size and shape of the retained choroid about the macula or the modifications in the retinal and choroidal

1. Cutler, C. W.: Drei ungewöhnliche Fälle von Retino-choroidal Degeneration, Arch. f. Augenh. **30**:117, 1894-1895.

2. Fuchs, E.: Ueber zwei der Retinitis pigmentosa verwandte Krankheiten (Retinitis punctata albescens und Atrophia gyrata choroideæ et retinae), Arch. f. Augenh. **32**:11, 1896; Textbook of Ophthalmology, translated by A. Duane, ed. 8, Philadelphia, J. B. Lippincott Company, 1924, p. 747; Textbook of Ophthalmology, translated by E. V. L. Brown, ed. 10, Philadelphia, J. B. Lippincott Company, 1933, pp. 321 and 376-378.

3. Nettleship, E.: On Retinitis Pigmentosa and Allied Diseases, Roy. London Ophth. Hosp. Rep. **17**:1, 151 and 333, 1907-1908.

4. Bedell, A. J.: Choroideremia, Arch. Ophth. **17**:444 (March) 1937.

circulation. Many cases are similar but none are identical." In the discussion of the differential diagnosis, he said: ". . . gyrate atrophy of the choroid . . . is so distinctive that it should rarely, if ever, be confused with choroideremia, for the destroyed areas are so definitely peripheral that there is no early circumpapillary atrophy and no characteristic macular design."

The first case of choroideremia, presented by Mauthner,[5] was classified by Leber as a case of retinitis pigmentosa associated with extreme atrophy of the choroid. Alexander[6] reported a case of congenital absence of the choroid with retinitis pigmentosa. He stated that gyrate atrophy of the retina "differs from retinitis pigmentosa only in the excess of choroidal atrophy." McGuire[7] reported an atypical case of gyrate atrophy of the retina and choroid in which night blindness, consanguinity and changes in the retinal vessels were lacking. Holloway[8] in discussing this paper stated that "The borderlines between some of these conditions are none too well defined" and further that "since Fuchs' observations nearly all of the recorders have accepted his views as to the onset of the condition; that is, that the atrophy is primarily choroidal and proceeded from the finer ramifications of the small choroidal vessels."

Hartshorne[9] reported a case of "bilateral choroidal atrophy with pigment migration to the inner layers of the retinae without contraction of the fields and without night blindness in a seven-year-old female child. The condition was probably due to some biliary toxemia associated with one or more severe attacks of liver malfunction, followed by prolonged jaundice."

When this case was reported before the New York Academy of Medicine, Hartshorne[10] stated: "This case confirms Dr. Verhoeff's statement that changes in the choroid do not produce retinitis pigmentosa." The question of constitutional conditions acting as exciting conditions to evoke changes leading to retinitis pigmentosa was raised by Nettleship.[3]

Lyle[11] reported the occurrence of gyrate atrophy of the choroid and retina in a boy aged 12. The mother had night blindness and color blind-

5. Mauthner: Ein Fall von Choroideremia, Ber. d. naturw.-med. Ver. in Innsbruck **2**:191, 1871; cited by Bedell.[4]

6. Alexander, E. W.: Congenital Absence of the Choroid with Retinitis Pigmentosa and Report of a Case, Ophthalmology **6**:343, 1910.

7. McGuire, H. H.: Gyrate Atrophy of the Choroid and the Retina (Fuchs), Arch. Ophth. **8**:372 (Sept.) 1932.

8. Holloway, T. H., in discussion on McGuire.[7]

9. Hartshorne, I.: A Case of Choroidal Atrophy Without Night Blindness, Am. J. Ophth. **17**:945, 1934.

10. Hartshorne, I.: Choroidal Atrophy Without Night Blindness, Arch. Ophth. **12**:288 (Aug.) 1934.

11. Lyle, D. J.: "Moon Eye": Gyrate Atrophy of the Choroid and Retina, Am. J. Ophth. **15**:1165, 1932.

ness, with normal acuity, fundi and fields. A sister of the boy also had gyrate atrophy. In a more recent paper [12] he reported choroideremia in one cousin and gyrate atrophy in another cousin of consanguineous parents.

Mann,[13] referring to retinitis pigmentosa, stated: "In some of the affected pedigrees both gyrate atrophy, choroideremia and retinitis punctata albescens appear, showing that these are probably atypical forms of the same condition." Still referring to retinitis pigmentosa, she further stated: "We thus see that the condition can be produced by a variety of genetic disturbances, some of which appear to involve associated genes, others to be pure single mutations. Another point of genetic interest is the fact of the occurrence of atypical fundus changes (gyrate atrophy, choroideremia, macular degeneration, choroidal sclerosis, colloid bodies, etc.) in certain members of the affected stock." Speaking of choroideremia, she stated: "Mention has already been made of the association of choroideremia (absence of the choroid so that a part or the whole of the fundus presents a bright glistening white surface instead of the usual red) with retinitis pigmentosa and gyrate atrophy. It remains to consider the very rare sporadic cases of absence of the choroid. These are probably different from the foregoing, which are due to secondary atrophy. The sporadic ones are possibly purely developmental, the choriocapillaris having failed to form, not having disappeared secondarily."

Usher [14] regarded choroideremia and gyrate atrophy of the retina as different stages of the same disease.

REPORT OF CASES

CASE 1.—M. H., a white farmer aged 19, was first examined in 1923, at which time his complaints were poor vision and night blindness, which had been present as long as he could remember.

His parents were cousins. A paternal great uncle went entirely blind. Two brothers have similar symptoms. One was not examined because he was stubborn and would not come for the examination. This suggests a mental condition. The third brother is referred to in case 2. Two other brothers and three sisters are apparently normal.

The results of the external examination were normal. The visual acuity was 20/200 in each eye with a — 6.00 sph. ◠ — 1.00 cyl., ax. 180 for the right eye and a — 8.00 sph. ◠ — 1.00 cyl., ax. 180 for the left eye, and the patient could read Jaeger's test type 10. There were no evidences of lenticular changes. A diagnosis of retinitis pigmentosa was made.

12. Lyle, D. J.: Arrests in Embryologic Development as Factors in Vision: Brief Review of Embryology of the Eye with Associated Anomalies of Arrested Development, Arch. Ophth. **21:**1937 (June) 1939.

13. Mann, I.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, pp. 190, 192 and 196.

14. Usher, C. H.: A Few Hereditary Diseases of the Eye, Arch. Ophth. **14:**171 (July) 1935.
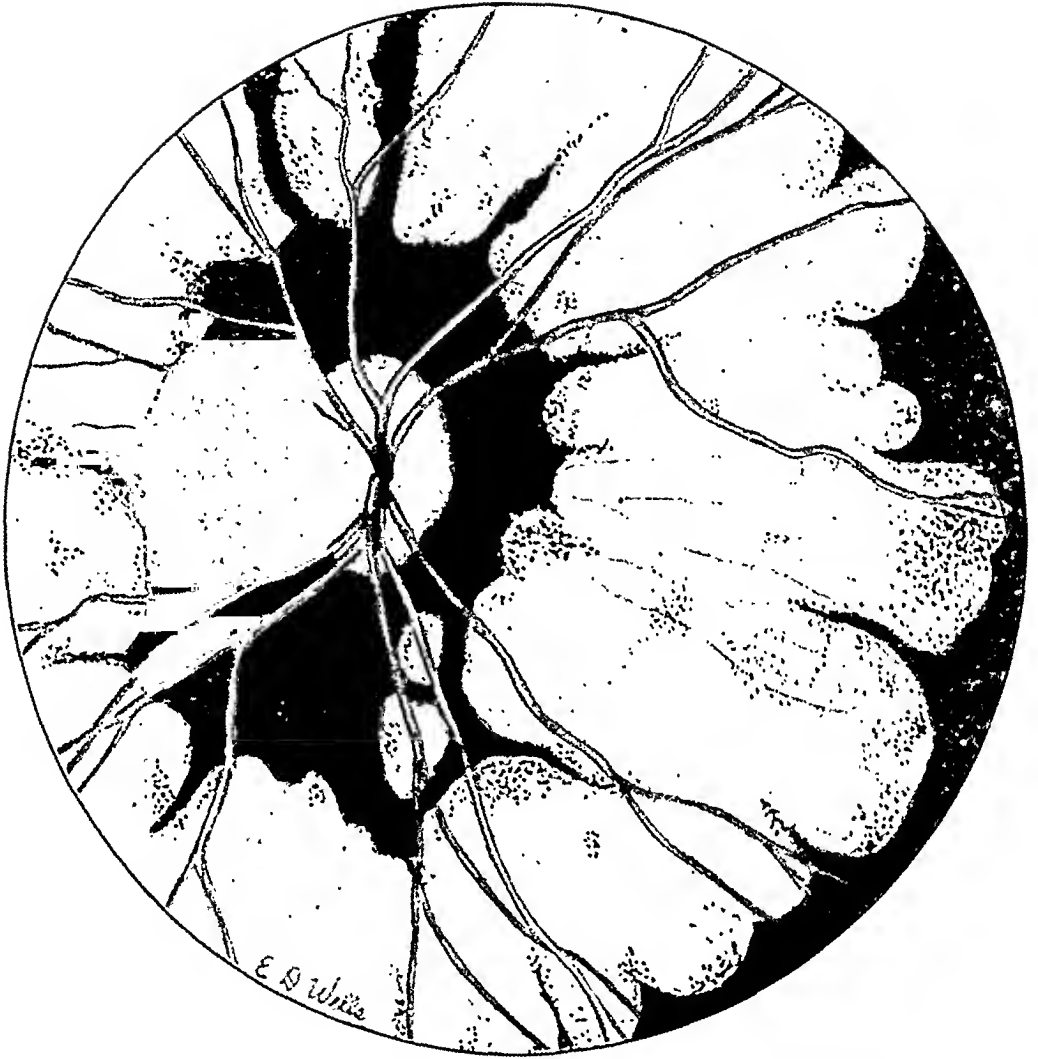
Fig. 1 (case 1).—Left fundus showing the disk surrounded by a ring of normal retina, a large amount of atrophy and diminution in size and number of the choroidal vessels.

In 1929 with homatropine cycloplegia the visual acuity was 20/100 in the right eye with a — 5.00 sph. ⊃ —2.00 cyl., ax. 180 and 20/70-1 in the left eye with a — 5.50 sph. ⊃ —3.50 cyl., ax. 180. At this time the notation was made of large areas of choroidal atrophy in each eye.

In 1934 he was seen at the clinic of the Episcopal Eye, Ear and Throat Hospital; there was a mature cataract in the right eye. In the left eye there was a posterior cortical cataract similar to that seen in association with retinitis pigmentosa. The visual acuity in the right eye was reduced to perception of light with poor projection of light. The corrected visual acuity in the left eye was 20/70, and a note was made by one of the resident staff of "tremendous patches of myopic choroiditis." The chief of the clinic diagnosed the condition as retinitis pigmentosa. On Oct. 30, 1934 the right lens was extracted in its capsule.

In 1936 the visual acuity was 20/70 — 1 (very slowly) in the right eye with a + 6.00 sph. ⊃ + 4.00 cyl., ax. 120 and 20/100 in the left eye with a — 6.00 sph. ⊃ — 4.00 cyl., ax. 170. The patient was able to read Jaeger's test type 7 with the right eye with a + 9.00 sphere and cylinder and Jaeger's test type 6 with

A   B

Fig. 2.—*A*, right fundus of the patient in case 1 in 1937, showing the patch of normal retina on the temporal side of the blurred disk, the extensive atrophy on the nasal side and a projecting edge of the island of normal retina on the nasal side. The absence of choroidal vessels and the diminution in size and number of the retinal vessels are shown. *B* shows the left fundus of the patient in case 2.

the left eye with a — 3.00 sphere and cylinder. According to the notes made at this time, the following changes were observed: In the right eye there were many large floating opacities in the vitreous. The disk was not clearly outlined and was surrounded by white atrophic areas, except on the nasal side, where there was only partial absorption. There were three islands of normal retina, one on the nasal side, one on the temporal side and one above the disk. In the periphery the atrophy was complete except in the upper temporal quadrant, where there were a few scattered spots of pigment. In the upper temporal region there was little retinal and choroidal tissue remaining, and it looked similar to an extensive inactive choroiditis. The left eye was similar but difficult to see because of the posterior cortical changes in the lens, similar to those seen in retinitis pigmentosa.

The last examination in May 1939 showed essentially no change in the condition. The patient was able to distinguish a 1 mm. red and a 1 mm. blue test object but was unable to distinguish a 12 mm. green test object at 33 cm. The field in the right eye was reduced to almost the fixation point; that of the left eye was concentrically contracted to 8 degrees.

Physical examination showed that there was a mixed deafness with little involvement of the nerve, as evidenced by the nearly normal bone conduction. There was fixation of the stapes. The Wassermann reaction of the blood was repeatedly negative, as reported by different laboratories. The Wassermann reaction of the spinal fluid was negative. The blood sugar content during fasting was within normal limits.

The appearances of the fundi are shown in figures 1 and 2 *A*.

CASE 2.—P. H., the brother of the patient in case 1, presented a picture so similar that a repetition of the findings would be superfluous (fig. 2 *B*).

The fundi and visual acuity of the father (J. H.), the mother (M. H.) and one brother (K. H.) were normal.

SUMMARY

The literature on gyrate atrophy of the retina and choroid is reviewed. The condition is sufficiently rare that definite opinions as to the etiology, prognosis and treatment are not possible. Symptomatically, the condition resembles retinitis pigmentosa and choroideremia. The occurrence of gyrate atrophy in one cousin and choroideremia in another is significant (Lyle's case), as is the coexistence of absence of the choroid with retinitis pigmentosa (Alexander's case).

The cases of two siblings of consanguineous parents are reported in which a diagnosis of retinitis pigmentosa was made; six years later atrophic changes were noted, and eleven years later a diagnosis of gyrate atrophy of the retina and choroid was made. The characteristic features are reduced visual acuity, night blindness, contracted fields, progressive atrophy of the retina and choroid and complicating cataract. The cases lend strong support to the possible association of retinitis pigmentosa and gyrate atrophy.

The appearance of the fundi suggests the possible development of complete atrophy of the retina and choroid, so that the appearance of choroideremia may eventually ensue. If this should occur, it would confirm Bedell's statement that choroideremia "must not be considered as a congenital condition but as a dissolution of that membrane."

RETINITIS PIGMENTOSA

ETIOLOGIC AND CLINICAL IMPLICATIONS BASED ON TWENTY-ONE CASES

ROBERT C. MOEHLIG, M.D.

AND

RALPH H. PINO, M.D.

DETROIT

Twenty-one cases of retinitis pigmentosa in which the familial history and certain physical characteristics were studied form the basis of this report. Because of the well known effect of the pituitary gland (pars intermedia) on the pigmentary system, it was felt that some clinical characteristics might be present which would link this gland with retinitis pigmentosa. Furthermore, owing to certain clinical findings, the embryologic development of the hypothalamic-pituitary and optic systems was thought to be of importance as giving a clue to the causation of this disease.

Involvement of the pituitary gland and the diencephalon in an etiologic role has been thought of by several investigators (Mamola and Bellina,[1] Schupfer,[2] Viallefont[3] and others).

The essential features pertinent to the discussion are given in the accompanying table.

The ages of the patients ranged from 8 to 51 years, the average age being 32.2 years.

There were 11 males (52.4 per cent) and 10 females (47.6 per cent).

One hundred per cent had a high arched palate.

Twenty (95 per cent) had dark hair (19 had brown and 1 had black hair) and only 1 (5 per cent) had light (blond) hair. The patient with light hair was a boy aged 8, and his hair was getting darker.

Three patients (14 per cent) were offspring of consanguineous parents.

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1. Mamola, P., and Bellina, G.: Nuove vedute sulla patogenesi e sulla terapia della retinite pigmentosa, Rassegna ital. d'ottal. 4:699-724 (Nov.-Dec.) 1935.

2. Schupfer, F.: Sulla retinite pigmentosa con particolare riguardo alla sua patogenesi, Boll. d'ocul. 15:189-262 (Feb.) 1936.

3. Viallefont, H.: Sur les rapports de l'hypophyse et de la rétine à propos de certaines rétinites pigmentaires, Ann. d'ocul. 173:33-42 (Jan.) 1936.

Summary of Twenty-One Cases of Retinitis Pigmentosa

Case No.	Name	Age	Sex	Height, Inches	Familial Height, Inches	Color of Hair	Familial History	Goiter	Special Findings
1	W. E.	27	♂	70	Father, 73 Brother, 72	Brown	Mother has migraine	Yes; operated on for toxic goiter	High arched palate; marked hirsutism of whole body; kyphosis
2	E. F.	37	♂	68½	Father, 70 2 brothers, 73 mother's people very tall	Brown	Mother has migraine; paternal grandfather had recurring iritis; paternal aunt was blind from retinitis pigmentosa	Yes; bilateral adenoma	High arched palate; prognathic jaw; hirsutism of body
3	M. H.	27	♀	65½	Father, 73 Brother, 72	Brown	One sister has migraine; 1 sister never menstruated; 1 sister had a goiter	Yes; adenoma	High arched palate; menstruates scantily for 1 day
4	H. B.	20	♀	66	Father, 72½	Brown	Mother has a large brown pigmented area on dorsum of left hand 4 by 2 inches (10 by 5 cm.) in diameter	Yes; adenoma on right side	High arched palate
5	J. H.	29	♂	72	Father, 70½	Brown	Mother had migraine, high blood pressure and a goiter; patient has migraine	Yes; bilateral adenoma	High arched palate; brown moles on back and right forearm
6	M. L.	40	♂	74	Father, 73 Mother, 68 Brother, 70	Brown	Mother died of nephritis, had asthma and high blood pressure; patient has migraine	Yes; adenoma of right lobe	High arched palate; bluish pigmented nevi on right side of chest and also on the outer surface of left malleolus
7	O. C.	22	♂	72	Father, 72	Brown	Not obtained; patient has migraine	Yes; bilateral adenoma	High arched palate
8	F. S.	43	♀	65½	Father, 72	Brown	Father had "eye trouble"; died of apoplexy at the age of 63; paternal uncle totally blind from retinitis pigmentosa	Yes; had thyroidectomy for toxic adenomatous goiter	High arched palate
9	C. J.	53	♂	65	Brother, 72 2 sisters "close to 72 inches"	Brown	Two sisters have migraine; patient's daughter has migraine; maternal grandmother totally blind; cause unknown	Yes; adenoma on right side	High arched palate; marked hirsutism of whole body
10	R. C.	22	♀	63 (weight 150 lb. [68 Kg.])	Father, 71 Brother, 71	Brown	Father and mother are second cousins; another has migraine and otosclerosis	Yes; small adenoma on right side	High arched palate; hirsutism of body; male distribution of pubic hair; tendency to lipodystrophy; obese

No.	Initials	Age	Sex	Height	Normal heights	Family history	Thyroid	Other
11	J. M.	59	♀	64	Brown	Father and mother were first cousins; sister has otosclerosis; patient was born deaf	Yes; large adenoma on left side	High arched palate; trace of sugar in urine
12	D. S.	51	♂	76½	Black	Father, 70 / Brother, 74 / Sister, 68	Father and mother were first cousins; father had cataracts; mother died of diabetes; brother has retinitis pigmentosa; sister of mother totally blind from unknown cause; sister has migraine; patient has migraine	No	High arched palate; kyphosis of spine; prognathic jaw
13	E. H.	22	♀	66	Brown	Father, 72 / Mother, 68	Brother has retinitis pigmentosa; patient has migraine and chronic eczema of both hands	Yes; adenoma	High arched palate; enamel defects of teeth; cyst of right breast
14	E. M.	17	♂	71½	Brown	One brother, 72 / One brother, 71½	Maternal grandmother totally blind from unknown cause; brother has migraine	No	High arched palate; prognathic jaw; female distribution of pubic hair
15	F. S.	51	♀	64½	Brown	No tallness in family	Maternal grandfather was blind from unknown cause; mother had migraine; patient had migraine	Yes	High arched palate; brownish pigmentation of both arms; had fibroid tumor of uterus
16	H. B.	26	♂	72	Brown	Father, 72 / Mother, 70	Father had migraine; patient has migraine	Yes	High arched palate; brown pigment on left hand
17	H. W.	35	♂	70½	Brown	No tallness	Mother had migraine; patient has migraine	Toxic goiter; operation	High arched palate
18	J. B.	54	♀	64½	Brown	Father, 72 / Two sons, 72	Two sons have migraine; mother had migraine; maternal cousin totally blind; patient has migraine	Yes	High arched palate; large brown pigmented area on abdomen
19	M. H.	19	♀	63	Brown	Father, 71	Mother has cataracts; maternal grandfather had cataracts; father has migraine; patient has migraine	Yes	High arched palate
20	K. M.	26	♀	63	Brown	Brother, 72 / Brother, 71	Brother has migraine; patient has migraine; brother had thyroidectomy for toxic goiter	Yes	High arched palate; several pigmented moles on body; exostosis of left hip
21 R. H. (brother of patient in case 13)		8	♂	51	Blond	Father, 72 / Mother, 68	Sister has retinitis pigmentosa; sister has migraine	No	High arched palate

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The heights of the males ranged from 51 to 76½ inches (129.54 to 194.31 cm.), with an average of 70⅕ inches (178.3 cm.), the average being lowered 2⅕ inches (5.58 cm.) by the height of the 8 year old boy. The heights of the female patients ranged from 60 to 66 inches (152.11 to 167.64 cm.), with an average of 64¼ inches (163.2 cm.).

The familial heights showed a tendency to tallness, 17 of the 21 patients (80 per cent) having one or more members in the immediate family who were 71 inches (180.34 cm.) or more in height.

Fifteen patients (71 per cent) gave a familial history of migraine, and 11 patients (52 per cent) themselves had migraine.

Eighteen patients (85.7 per cent) had goiters of the adenomatous type. Three (14 per cent) had toxic adenomatous goiters which required thyroidectomy.

Nine patients (42 per cent) gave a familial history of ocular disturbances, and 5 (23.8 per cent), a familial history of retinitis pigmentosa. Five (23.8 per cent) had some member of the family, but not of the immediate family, who was totally blind.

Four patients (19 per cent) had marked hirsutism of the body (all brunettes).

DATA TO SUPPORT THE RELATION OF RETINITIS PIGMENTOSA TO PITUITARY DYSFUNCTION

The diagnosis of retinitis pigmentosa (except in referred cases) was made by the one of us who specializes in ophthalmology (R. H. P.), and the general check-up was made by the one interested in endocrinology (R. C. M.).[4] Tubular vision was present in several of the patients.

There was nothing significant in the ages; the youngest patient was a boy aged 8, whose sister, aged 17, also suffered from the same condition.

The percentage of male and female patients with retinitis pigmentosa was about equal. Males are as a rule more often affected than females, but in this series such was not the case.

What seems significant is the fact that all, or 100 per cent of the patients, had a high arched palate.

This common factor may be exceedingly useful in determining the etiologic factor. The embryologic development of the hard palate is responsible for the high arching of the palate. Furthermore, it is generally accepted that the pituitary gland develops from the ectoderm in

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4. Drs. Parker Heath, Don Campbell, Duncan Campbell, Malcolm Campbell, W. S. Summers and Hermon Sanderson gave permission for us to include data on patients referred to one of us (R. C. M.).

the roof of the mouth. Thus this gland would be involved in the abnormal development of the latter structure. Data to be presented suggest this to be the case.

Tilney,[5] in a splendid review of the glands of the brain, stated:

The origin of the hypophysis, from the lowest vertebrates to man, is constant in its fundamental constituents and mode of development. The organ arises from two specialized sources of ectoderm, the somatic ectoderm in or about the region of the mouth and the neural ectoderm in the floor of the third ventricle. Processes from these two ectodermal sources approach and meet each other to form the hypophysis.

Proceeding further, it is noted that the diencephalon, which consists of the epithalamus, thalmus and hypothalmus, and the eye have close embryologic developmental connections. Zondek,[6] speaking of the embryologic development, said:

The lateral walls of the primary cerebral vesicles are protruded to form the optic vesicles. The optic stalks (future optic nerves) connect the optic vesicles from which the diencephalon subsequently develops. Embryologically the diencephalon is also connected with the pituitary body—whilst the anterior (glandular) pituitary lobe arises from a protrusion (Rathke's pouch, pituitary pouch). This grows upwards towards the floor of the diencephalon from which at the same time a funnel-shaped excrescence develops which comes in touch with the apex of the pituitary pouch. The two coalesce to form the pituitary body. Between these two parts of the gland the pars intermedia is formed by the production of glandular tubuli from the dorsal surface of the pituitary cavity; this portion is well developed in animals but is only rudimentary in man.

The nerve fiber connections between the pituitary gland and the hypothalamus have been ably reviewed by Fisher, Ingram and Ranson [7] and more recently by Ingram [8]; the latter author gave a thorough and comprehensive review of the experimental data as they relate to the hypothalamus. Grinker,[9] speaking of the hypothalamus, said:

Related directly to the hypophysis and indirectly to other glands of internal secretion, the hypothalamus, (1) regulates endocrine functions and their interrelations; (2) regulates and integrates conservating autonomic functions; (3) is

5. Tilney, F.: The Glands of the Brain with Especial Reference to the Pituitary Gland, A. Research Nerv. & Ment. Dis., Proc. (1936) **17**:3-47, 1938.

6. Zondek, H.: The Diseases of The Endocrine Glands, Baltimore, William Wood & Company, 1935.

7. Fisher, C.; Ingram, W. R., and Ranson, S. W.: Diabetes Insipidus and the Neuro-Hormonal Control of Water Balance: A Contribution to the Structure and Function of the Hypothalamico-Hypophyseal System, Ann Arbor, Mich., Edwards Brothers, Inc., 1938.

8. Ingram, W. R.: The Hypothalamus: A Review of the Experimental Data, Psychosom. Med. **1**:48-91 (Jan.) 1939.

9. Grinker, R. R.: Hypothalamic Functions in Psychosomatic Interrelations, Psychosom. Med. **1**:19-47 (Jan.) 1939.

concerned with teleologically defensive and protective reactions which we term emotional expressions and (4) influences the activity of the cerebral cortex in regulation of degree of wakefulness and excitation.

The close embryologic and anatomic association between the pituitary gland, hypothalamus and eye also suggests that there is a close physiologic connection between these structures. Riseases of the pituitary gland may produce ocular disturbances other than by direct local pressure effects, namely, by hormonal influences. Zondek [6] was of this opinion, for he said that retinitis pigmentosa, both the typical and the atypical form, together with disturbances in the pituitary-diencephalic region, is typical for the Laurence-Biedl syndrome. Sometimes it is true, he said, that retinitis pigmentosa may be the sole clinical evidence of diencephalic disturbance. Yet even in such cases thorough investigation may reveal some disturbances, e. g., in metabolism, which point to a disease of the pituitary-diencephalic system. In such cases the assumption will be justified that degenerative processes have gradually spread over the whole region which extends from the sides and floor of the third ventricle through the optic nerves into the eyes, more especially the retinas.

Certain facts help to establish a relation between the pituitary gland and the pigments of the eye. It has been known for some time that the posterior lobe of the pituitary gland (pars intermedia) contains a melanophoric stimulant (Allen,[10] Spaeth,[11] Hogben and Winton [12] and others).

Zondek [13] reviewed the evidence pointing to the chromatophoric principle of the pars intermedia of the pituitary gland. All authors agree that this principle is produced in the intermediate lobe. The hormone leaves the gland by the path of the pituitary stalk and is demonstrable only in the walls of the third ventricle, where the vegetative centers are located, and nowhere else. Zondek and Krohn [14] employed the erythrophore reaction in a certain fish to demonstrate the presence of chromat-

10. Allen, B. M.: Source of the Pigmentary Hormone in the Anterior Hypophysis, Proc. Soc. Exper. Biol. & Med. **27:**504, 1930.

11. Spaeth, R. A.: Concerning a New Method for the Biological Standardization of Pituitary Extract and Other Drugs, J. Pharmacol. & Exper. Therap. **11:**209-219 (April) 1918.

12. Hogben, L. T., and Winton, F. R.: The Pigmentary Effector System: I. Reaction of Frog's Melanophores to Pituitary Extract, Proc. Roy. Soc., London **93:**318-329, 1921-1922.

13. Zondek, B.: Chromatophorotropic Principle of the Pars Intermedia of the Pituitary, in Glandular Physiology and Therapy, A Symposium, Chicago, American Medical Association, 1935, chap. 9.

14. Zondek, B., and Krohn, H.: Hormon des Zwischenlappens der Hypophyse (Intermedin), Naturwissenschaften **8:**134, 1932; Hormon des Zwischenlappens der Hypophyse (Intermedin) ; die Rotfärbung der Elritze als Testobject, Klin. Wchnschr. **11:**403 (March 5) 1932.

ophore-stimulating hormone. When a solution of posterior pituitary is injected into a certain minnow (Phoxinus laevis) a characteristic red colorization appears within a half an hour at the point of the attachment of the thoracic abdominal and anal fins. It has been shown to be "hormone specific." These authors called the hormone "intermedin."

Van Dyke [15] stated:

Hypophysectomy in the normal frog tadpole results in a concentration of the melanosomes, particularly in the melanophores of the epidermis, and a dispersion of the pigment granules in the xantholeucophores. Both of these changes are responsible for the silvery (albino) appearance of the hypophysectomized tadpoles. Smith found that hypophysectomy in the tadpole is followed by a reduction both in the amount of intracellular melanin and in the number of epidermal melanophores.

Injection of solution of posterior pituitary or the transplantation of the pars intermedia (adult frogs) into normal or hypophysectomized tadpoles causes a marked dispersion of the melanosomes. According to Van Dyke:

If frogs are kept in complete darkness for about 20 minutes, the melanosomes become concentrated and the hormone causing their dispersion is said almost to disappear. Melanosome dispersion has been caused by the following tissues or fluids or extracts of these: hypothalamus, cerebrospinal fluid (lumbar fluid is often reported not to have an effect) *eye (and aqueous humor)* blood, urine, and colostrum.

The influence of the eye and aqueous humor extracts in producing a dispersion of melanosomes is of interest in regard to retinitis pigmentosa and pigmentary disturbances of the eye. It would indicate that secretion of the pars intermedia may be contained in the eye.

In some amphibia light may directly affect the chromatophores; the melanophores of the frog are altered chiefly because of optic stimuli. The removal of the eyes, but not spinal transection, abolishes the changes in the chromatophores, adapting animals to light or dark background (Van Dyke).

Jores [16] and Jores and Hotop [17] stated that the instillation of melanophore-stimulating hormone into the eye shortened the time required for adapting the eye to darkness. These investigators were of the opinion that the pituitary gland of animals with nocturnal habits contained a higher concentration of the hormone than that of animals with diurnal

15. Van Dyke, H. B.: The Physiology and Pharmacology of the Pituitary Body, Chicago, University of Chicago Press, 1936.

16. Jores, A.: Änderungen des Hormongehaltes der Hypophyse mit dem Wechsel von Licht und Dunkelheit, Klin. Wchnschr. **48**:1713-1716 (Nov. 30) 1935.

17. Jores, A., and Hotop, H.: Vergliechende Untersuchungen über den Gehalt verschiedener Tierhypophysen an Melanophoren und Erythrophorenhormon, Ztschr. f. vergl. Physiol. **20**:699-701, 1934.

habits. Jores found that darkness produced an increase in the melano-phore-hormone content of the pituitary gland as well as in its blood-pressure raising and uterine-stimulating principles. Rodewald [18] confirmed these findings in the frog. Jores [17] made the following observations:

> When an animal is brought into darkness, there is an immediate fall in the active melanophore hormone content of the pituitary. The content of the blood pressure-hormone in the posterior lobe is next to decrease followed within one-half to one hour by an increase of double the original amount. This transposition is affected via the eye. It has been known for some time that in the eyeless frog, the ability of adaptiveness to the ground or substratum [*Untergrund*] was disturbed. Von Greving found this to be due to a direct nervous connection between the eye and the pituitary.

Rodewald [18] reported that she could produce the characteristics of a light-adapted animal in a dark-adapted animal by electrical stimulation of the optic nerve.

Jores [17] concluded that light produces certain effects on the endocrine system, but that this is not the sole factor. He applied his studies of the daily periodic variations to biology. There is a certain periodicity to the daily mechanism of life, such as variations in temperature, metabolism, concentraton of urine and sleep. Periodic changes have been noted during the twenty-four hour cycle in plant life, where the opening and closing of certain plant leaves occur at different periods of the day.

The pigment cells seem to be a derivative of the mesoderm. Ewing [19] said:

> It follows that there must be a close parallel between the physiological formation of pigments and that seen in pathological conditions such as melanosarcoma. Much evidence has been collected which points to the metabolic origin of pigment. The evidence accumulating in recent years from the comparative study of the physiology of the color function in the animal kingdom is a very formidable argument in favor of the specific mesoblastic nature of the chromatophores.

Bloch [20] stated that in his opinion the chromatophores are of mesodermal origin.

Ribbert [21] was one of the original defenders of the view that connective tissue gives off pigment cells; he likewise believed that the nerve elements and melanotic pigment in general are derived from chromatophores and are therefore mesodermal in origin and that these cells stand in direct physiologic relation to pigment formation.

18. Rodewald, W.: Die Wirkung des Lichtes auf die Hypophyse von Rana temporaria L., Ztschr. f. vergl. Physiol. **21**:767-800, 1935.

19. Ewing, J.: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922.

20. Bloch, B.: Personal communication to the authors.

21. Ribbert, cited by Ewing.[19]

The late Mr. Judd of Dr. Pino's staff, after extensive dissections of the eyes of embryo chicks in all stages of development, stated his impressions as follows:

. . . Even though the whole structure of the the retina seems to be of ectodermal origin, the pigment layer separates as readily from the adjacent retinal layer as any separate type of tissue might do in dissection, and that, as is easily demonstrated by the aid of very little light stimulation, the pigment layer meshes with the rod and cone layer. In all mechanical respects it appears as distinctly separate an organ from the retina as is the mesodermal choroid. This condition obtains in the embryological tissue of the chick and frog. Embryologists dealing with human material stress the fact that the pigment epithelium of the retina develops from the outer wall of the optic cup, showing lack of cytoplasmic continuity with the retina until at least a very late stage of development.

But if all pigment originates in the mesoderm as a result of metabolic processes, then one must conclude that the pigment migrates from the mesoderm and is brought to the ectodermal retina.

The melanophore hormone of the pituitary gland probably has nothing to do with the production of pigment which follows inflammatory conditions of the eye. But, as previously noted, extracts of the eye and aqueous humor are capable of producing a dispersion of melanosomes, suggesting that this hormone may be present in the eye. Collin [22] described nerve fibers going to the pituitary gland from the supraoptic nucleus, central gray substance and tuber cinereum. He was of the opinion that the retinopituitary connections or photopituitary fibers related to pigmentary functions and to the thalamus anatomically explain the mechanism for the influence of light on the sexual process. Kylin [23] described a path or duct from the third ventricle to the pituitary gland via the pituitary stalk.

Bissonnette [24] said that there is increasing evidence of the induction of physiologic and cytologic changes in the pituitary gland by nervous excitation and some evidence for such changes in response to modified exposures to light. He found at the crest of sexual activity vacuoles in both the basophils and the eosinophils of the anterior lobe like those in "castration" cells. The results suggested that one of these types of cell secretes a hormone controlling the interstitial cells of the testis and the other a hormone stimulating the germ cells. Others, however, using other animals, have found a seasonal cycle of the anterior lobe.

In connection with the latter statement it is interesting to note the hibernation of animals.

22. Collin, R.: Sur l'existence probable d'une voie réflexe courte opto-hypothalamo-pituitaire, Compt. rend. Soc. de biol. **118**:1560-1562, 1935.

23. Kylin, E.: Ductus hypophyseo-cerebralis. Beitrag zur Frage der Sekretion der Hypophyse, Klin. Wchnschr. **14**:347 (March 9) 1935.

24. Bissonnette, T. H.: The Influence of Light upon Pituitary Activity, A. Research Nerv. & Ment. Dis., Proc. (1936) **17**:361-376, 1938.

Cushing and Goetsch [25] advanced the hypothesis of the seasonal nature of hibernation due to polyglandular inactivity as the etiologic factor. Recently Foster, Foster and Meyer,[26] in reviewing the influence of the endocrine glands on hibernation, concluded that their findings suggested inactivity of the pituitary gland as the primary factor responsible for the phenomena of hibernation.

Zondek and Bier [27] said that animals can be brought out of their hibernating state by placing them in artificial light and heat. Pregnancy is at a standstill during the hibernating period of the bat but proceeds normally when the animal is placed in artificial light and heat.

It is well established that during the hibernating state of animals the chromophobes are hyperplastic. This state is comparable to the colloid, or resting, state of the thyroid gland associated with myxedema or hypothyroidism. It is the opinion of one of us (R. C. M.) that the ordinary type of Fröhlich's syndrome is due to hyperplasia of the chromophobes. In animals when normal hibernation ends because of cosmic or other influences, the hyperplasia of the chromophobes is replaced by hyperplasia of the chromophils, and the animal goes into estrus, with consequent metabolic and cellular activity.

The cyclic variation of symptoms of ulcer suggests that the season of the year may influence the hypothalmic-hypophysial system. This would tend to bear out Cushing's [28] neurogenic hypothesis of peptic ulcer as due to a disturbance in the interbrain area, since the rhythmic variation of endocrine function is not unlikely. His clinical experience with tumors of the midbrain area associated with peptic ulcer is suggestive. Furthermore, the beneficial effect of sunshine in certain diseases makes it not unlikely that the mechanism operates via the hypothalamic-hypophysial system. The influence of the pituitary gland on the skeletal system suggests that activation of this gland by sunshine may be the answer as to why this form of therapy benefits rickets and other allied disorders.

It is not within our province to discuss the close association between sunshine, vitamins and the hormones, but a physiologic relation, especially in conjunction with ocular pigmentary disturbances, such as xerophthalmia and retinitis pigmentosa, is obvious.

25. Cushing, H., and Goetsch, H. E.: Concerning the Secretion of the Infundibular Lobe of the Pituitary Body and Its Presence in the Cerebrospinal Fluid, Am. J. Physiol. **27**:60-86, 1910.

26. Foster, M. A.; Foster, R. C., and Meyer, R. K.: Hibernation and the Endocrines, Endocrinology **24**:603-613 (May) 1939.

27. Zondek, H., and Bier, A.: Hypophyse und Schlaf, Klin. Wchnschr. **11**: 760-762 (April 30) 1932.

28. Cushing, H.: Pituitary Body, Hypothalamus and Parasympathetic System, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

The rhythmic cycle of pituitary cytologic changes has also been found by Zahl,[29] who noted that the acidophils in frogs were in greatest number and with the most abundant granules and fuchsinophil droplets in spring and early summer. They were less numerous in late summer and increased gradually in autumn and winter, to discharge again in spring.

Florentin and Stutinski [30] found that when frogs were kept in a dark room the anterior lobe of the pituitary gland soon lost its chromophobes and that only a few basophils and many acidophils remained. The pituitary gland was in a state of arrested function and showed the effects of lack of photopituitary reflexes.

Bissonnette,[24] in his conclusions, stated:

All of the above studies show effects of light and darkness, and even of specific wave-lengths of light on some animals, mediated by the eyes, optic nerves, and pituitary and accompanied by both cytological and physiological changes in the gland, and in pituitary activity. These types of changes vary in different species, often in correlation with changes induced by other factors in the environment.

We require much further study of these photopituitary reactions in many more animals before we can arrive at any very broad generalizations. But we already know that in many cases the daily period of light, its intensity, and its wave-length control and modify pituitary activity.

It is most reasonable to suppose, therefore, that girls in the tropics would menstruate and mature earlier than those in temperate and cold zones.

If one grants that the pituitary gland is related to the formation of pigment, then the activity of the melanophore hormone of the Negro would, pari passu, be greater than that of the Caucasian. The Negro, at one time, probably possessed a very active pituitary gland. Even today this seems to be true. Freeman,[31] for instance, studied the relation of the weight of the whole pituitary gland of the male to weight, stature and race. He said that the weight of the pituitary gland is better correlated with body-weight than with stature and that the pituitary gland of the Negro is heavier than that of the Caucasian if the weights of the pituitary glands of persons of the same sex are compared.

For some time one of us (R. C. M.) has stressed that the pituitary gland has a selective action on mesodermal tissues. If this is true, then the heavier pituitary gland of the Negro would by analogy produce

29. Zahl, P. A.: Cytological Changes in Frog Pituitary Considered in Reference to Sexual Periodicity, Proc. Soc. Exper. Biol. & Med. **33**:56-58, 1935.

30. Florentin, P., and Stutinski, F.: Modifications cytologiques de la glande pituitaire des grenouilles maintenues à l'obscurité, Compt. rend. Soc. de biol. **122**: 674-675, 1936.

31. Freeman, W.: The Weight of the Endocrine Glands: Biometrical Studies in Psychiatry, Human Biol. **6**:489-523 (Sept.) 1934.

certain peculiarities in the mesoderm of the Negro that would make this layer and its derivatives unique when compared with those in the white race. Details of this have been given elsewhere.[32]

Originally the Negro possessed a well developed mesoderm, and the ectodermal structures, such as the nervous system, were in comparison less developed.

The mesoderm was necessary for the development of muscular strength, the skeletal system, immunity and procreative powers. The Negro race is phylogenetically a closer approach to primitive man than the white race. Of particular importance is the fact that a white person with acromegaly takes on the physical characteristics of the Negro. The white man reverts to the primitive type. Keith [33] said:

I came to the conclusion then, which prolonged observation has gone to confirm, that the cranial and facial features of primitive man and those of acromegalic men and women are of the same nature—only in primitive man they were produced by a normal or physiological action, whereas in the acromegalic they are the result of an abnormal or pathological action.

Furthermore, he added:

There still lurks in the body of modern man the machinery which fashioned the ample features of Rhodesian man and which can be awakened under conditions of disease. It is the same machinery which determines the more exaggerated degree of bestial strength seen in the face of the gorilla.

Peculiarly enough, but readily understandable, is the fact that the hyperpituitary states, acromegaly and the pituitary basophilism of Cushing, are found almost exclusively in the brunette. Dark-complexioned females with hirsutism are more apt to have menstrual disturbances than the blond, and the latter are more apt to suffer from sunburn.

As previously stated, the mesodermal layer of the Negro has certain peculiarities as compared to the white person. It will be noted that when disease attacks the Negro, it most frequently does so in the mesoderm, whereas the ectoderm is relatively immune.

We cannot go into any detailed or statistical study which proves this, but even a cursory examination will show that the incidence of disease of mesodermal tissues is usually high for the Negro.

It is a generally accepted fact that the Negro has a tendency to connective tissue overgrowth, illustrated by the frequency of keloids, neurofibromas and fibroid tumors of the uterus. Disturbances in the bones of the Negro are unusually common, such as rickets, osteomalacia, gummas and yaws.

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32. Moehlig, R. C.: The Mesoderm of the Negro, Am. J. Phys. Anthropol. **22**: 297-314, 1937.

33. Keith, A.: New Discoveries Relating to the Antiquity of Man, New York, W. W. Norton & Company, Inc., 1934.

The hematopoietic system shows singular characteristics. While pernicious anemia, the leukemias and thrombocytopenic purpura are all rare diseases in the Negro, sickle cell anemia is a disease limited almost exclusively to this race. Melanosarcoma is also a rare disease in the Negro.

The foregoing diseases are but a few examples which show the differences in the mesoderm of the Negro and of the white races.

It is of interest that posterior pituitary extract has a selective action on certain tissues, viz., smooth muscle of the uterus, intestines, kidneys and capillaries. These are all mesodermal derivatives. It would seem therefore that its effect on the melanophores would add strength to the argument that the mesoderm gives rise to the pigment cells.

Fifteen patients, or 71 per cent, gave a familial history of migraine, and 11, or 52 per cent, themselves had migraine.

The average height of the male patients was 72.8 inches, and 16, or 76 per cent of all the patients, had one or more members in the immediate family who were 72 inches or more in height. Böck and Risak[34] reported a case of retinitis pigmentosa in a tall patient with a disturbance of the midbrain. Naturally tallness in the male patients with retinitis pigmentosa would point to the pituitary gland as the cause of the skeletal overgrowth. One of our patients (case 12) with tubular vision was 76.5 inches in height. His father and mother were first cousins.

This tendency to tallness is greater than is found in an average sampling of the population. These figures correspond closely with a previous report one of us (R. C. M.)[35] made on 100 patients with migraine. It was therein reported that 70 per cent of 51 female and 80 per cent of 21 male patients with migraine had one or more members in the immediate family who were 72 inches or more in height.

Furthermore, all of the patients with migraine had an enlarged thyroid gland. Due allowance was to be made, however, for the fact that these patients lived in a goiter belt.

High cholesterol values (average 225 mg. per hundred cubic centimeters of blood) were found in the migrainous patients, and Rémond and Rouzaud[36] also found this to be true. Concerning this, Riley[37] said:

"One item has received more or less substantiation, that is, the uni- formly increased cholesterol content of the blood."

34. Böck, J., and Risak, E.: Retinitis pigmentosa und Hochwachs, Ztschr. f. Augenh. 84:48-58 (Aug.) 1934.

35. Moehlig, R. C.: Migraine: A Study Based on One Hundred Cases, Endocrinology 15:11-16 (Jan.-Feb.) 1931.

36. Rémond, A., and Rouzaud, J.: L'azotémie et la cholestérinémie chez les migraineux, Rev. de méd., Paris 38:97-112 (Feb.) 1921.

37. Riley, H. A.: Migraine, Bull. Neurol. Inst. New York 2:429 (Nov.) 1932.

Our findings of a high arched palate in all of our patients with retinitis pigmentosa and a high incidence of migraine and familial migraine is in harmony with the work of Riley, who noted malformation of the hard palate as well as congenital defects in the formation of the bones of the skeleton in migrainous patients. Balyeat [38] also found that malformation of the hard palate has not been an uncommon finding.

Ulrich,[39] in her study of 500 cases of migraine, recorded the occurrence of a general disharmony in bodily development: premature graying of the hair, abnormal growth and distribution of hair, confluent eyebrows, convergent or divergent strabismus, asymmetric distribution of the pigment in the iris, myelinated nerve fibers in the retina, color blindness, irregular and abnormal development of the forehead, supernumerary nipples, small or undescended testicles, microcephaly with normal intelligence, cervical ribs and inequality of the breasts. One of our patients with migraine and retinitis pigmentosa showed malformation of the skeleton and pigmentation on the arm and chest. Such malformations, and particularly the high arching of the palate, raise a question as to the causation. Are they the result of a developmental chromosomal defect? Does this arching of the palate indicate a disturbance in the development of the pituitary gland, since the anterior lobe originates from the roof of the mouth? We are inclined to believe that this is the case and that secondary pituitary hormonal effects are added to the primary developmental defects. The work of Mortimer [40] supports this view. He studied the influence of the pituitary gland and associated hormone factors in cranial growth. He investigated in particular the problem of the part played by the pituitary gland in cranial growth with a view to throwing light on the problem of human cranial dysplasia in its relation to pituitary dysfunction.

He reported on 494 dysplastic craniums in human beings. Sixty per cent of the patients who showed evidence of disturbance in cranial form and structure, presumably during the growth period, suffered subsequently at some time or another from a dyspituitarism that was recognized physiologically. This fact was taken to support the view that cranial dysplasia is probably produced by dyspituitarism and not by an autochthonous peculiarity of certain tissues in response to a normal secretion from the anterior lobe of the pituitary gland. That the cranial deformity resulted in response to abnormal pituitary function is reasonable, the presumption being that those persons in whom

38. Balyeat, R. M.: Migraine, Philadelphia, J. B. Lippincott Company, 1933.

39. Ulrich, M.: Beitrag zur Aetiologie und zur klinischen Stellung der Migräne, Monatschr. f. Psychiat. u. Neurol. **31**:134-203, 1912.

40. Mortimer, H.: The Influence of the Anterior Pituitary on Cranial Form and Structure and the Significance of Cranial Dysplasia in Clinical Diagnosis, A. Research Nerv. & Ment. Dis., Proc. (1936) **17**:222-238, 1938.

dyspituitarism is physiologically recognizable today and in whom cranial dysplasia also exists suffered also from a dyspituitarism at the time when cranial form and structure are most susceptible to hormonal growth influences. Mortimer went on to state that in cases in which a familial tendency to such deformity undoubtedly exists, a familial tendency to dyspituitarism may be suspected. The familial history as developed in our paper bears this out.

Several authors (Timme,[41] Deyl,[42] Leopold-Levi,[43] Halloran,[44] Kast[45] and others) have expressed the belief that swelling of the pituitary gland is the cause of migraine and accounts for the scotomas, scintillations and other visual disorders. Deyl[42] carried out his investigations on hundreds of cadavers in order to determine the actual anatomic relation between the possibilities of pressure of the pituitary gland on neighboring structures. He felt that the gland was capable of exerting pressure on the cavernous sinus and the structures contained within it. He thought that there was a transient increase in size of the gland during the migrainous attack. He also stated that tumors of the pituitary gland, such as found in association with acromegaly, often produce headaches of the migrainous type.

In our opinion, actual engorgement, congestion or change in size of the pituitary gland is not necessary to explain migraine, but it would be better understood on the basis of a change of function with alteration in the amount of hormonal secretion delivered to the system. Particularly does this seem true in the light of the newer developments, which show the close physiologic relations existing between the hypophysial-hypothalamic and optic systems.

The frequent incidence of goiter in the present series of patients with retinitis pigmentosa is of some significance. As already stated, this same high incidence of goiter was noted in a previous series of 100 patients with migraine.

Today many authors will ascribe the presence of the goiter to a primary hyperfunction of the pituitary gland with overproduction of its thyrotropic hormone. Others again may interpret the condition as being primary in the thyroid with secondary changes in the pituitary gland. One can marshal as many facts to support the argument one way as another, depending on on which horn of the dilemma one chooses to sit.

41. Timme, W.: Discussion of Migraine, Brit. M. J. 2:771 (Oct. 30) 1926.

42. Deyl, cited by Riley.[37]

43. Leopold-Levi, cited by Riley.[37]

44. Halloran, R. O.: Migraine: Pituitary Study, West Virginia M. J. 35: 233-236 (May) 1939.

45. Kast, L.: Headache from Viewpoint of Internist, Bull. New York Acad. Med. 1:149 (June) 1925.

Zaffke [46] reported that night blindness or the impairment of the dark adaptation is a symptom of vitamin A deficiency. He examined 21 patients with disturbances of the thyroid and found that in all typical cases of thyrotoxicosis the adaptation curve is pathologic and indicates night blindness. He expressed the belief that the night blindness which is observed in association with this disease is a result of the thyrogenic impairment of the liver, since severe thyrotoxicosis results in a damaged or impaired liver. The liver is an important storage organ for vitamin A. Wegelin [47] concluded from his histologic experiments on the rat's liver that there exists a definite antagonism between thyroxine and vitamin A in regard to glycogen content and in number of mitotic figures.

The disappearance of fat in the kidneys brought about by the administration of thyroxine is not counteracted by vitamin A.

Wohl and Feldman [48] studied patients with various endocrinopathies for vitamin A deficiency by means of the dark adaptation method. The group with disturbances of the thyroid gave the most consistent results, and the findings and other data reviewed in the paper suggest that the thyroid hormone is essential for conversion and storage of vitamin A.

The foregoing studies make the presence of a goiter in the majority of our patients with retinitis pigmentosa of importance. Three of the 21 had goiters of the toxic variety.

Nine patients (42 per cent) gave a familial history of ocular disturbances, such as cataracts; 5 (23.8 per cent) gave a familial history of retinitis pigmentosa, and 5 (23.8 per cent) reported blindness in the family.

Three patients (14 per cent) were offspring of consanguineous parents.

These findings would indicate a familial constitutional weakness due apparently to transmission in the eye genes.

The number of patients with hirsutism of the body, kyphosis of the spine and prognathic jaws is so few that in a small series such as this no real significance can be attached to these findings. Taken as a whole, however, one might hazard the opinion that a pituitary disturbance was present, since these characteristics are presented by persons with acromegaly.

Six patients (28 per cent) had areas of pigmentation on the body, but this number is also too small to be of any great significance, as a

46. Zaffke, K. H.: Hemeralopie als Symptom bei Thyreotoxicosen und Lebererkrankungen, Deutsches Arch. f. klin. Med. **183**:433-487, 1939.

47. Wegelin, C.: On the Antagonism Between Thyroxine and Vitamin A, West. J. Surg. **47**:147-154 (March) 1939.

48. Wohl, M. G., and Feldman, J. B.: Vitamin A Deficiency in Diseases of the Thyroid Gland: Its Detection by Dark Adaptation, Endocrinology **24**:389-396 (March) 1939.

sampling of the general population would probably approach this figure. It may, however, be an indication of a pigmentary metabolic disturbance associated with a retinal pigmentary disturbance.

If one were to grant the hypothesis of a pituitary disturbance as an etiologic factor, then does it represent a hypofunction or a hyperfunction of the gland? At one stage of the condition an overactivity of the gland may be assumed. This is based on the following facts: Ninety-five per cent of the patients had dark hair; there was a tendency to tallness among the male patients, with a high percentage of tallness in the immediate family of all patients; a high percentage of the patients gave a history of familial migraine, and about half of the patients had migraine; a high percentage had adenomatous goiters, while a small percentage had hirsutism of the body, kyphosis of the spine, prognathic jaws and areas of pigmentation on the body. Taken individually, any one or a few of the characteristics enumerated would mean little, but collectively they indicate that the pituitary gland was or is hyperactive. Such an assumption would denote overactive pigmentary metabolism with freeing of pigment deposit from the retina or the formation of new pigment.

If, on the other hand, it is assumed that the pituitary gland is underactive, then one can only postulate a failure of pigment fixation due to a lack of the chromatophorotropic hormone. It is our opinion that retinitis pigmentosa without pigment and retinitis albescens are probably due to a failure of the hormone of the posterior lobe (pars intermedia) of the pituitary gland. The lack of hormone would result in the failure of fixation of pigment in the retina.

Be that as it may, the argument that the pituitary gland is involved in retinitis pigmentosa receives support from the data submitted.

SUMMARY

A summary of the 21 cases of retinitis pigmentosa is given.

Because of the presence of a high arched palate in all the patients, stress is laid on the embryologic development of the palate, the pituitary gland, the diencephalon and the optic system.

Data are submitted which support the theory that the pituitary function is involved in retinitis pigmentosa.

Of course, the actual proof of this opinion would require studies of this hormone in the blood of these patients, but as yet such studies are not on a practical basis.

TONIC DEVIATIONS OF EYES PRODUCED BY MOVEMENTS OF HEAD

WITH SPECIAL REFERENCE TO OTOLITH REFLEXES; CLINICAL OBSERVATIONS

FRANK R. FORD, M.D.

AND

FRANK B. WALSH, M.D.

BALTIMORE

It has long been known that movements of the head produce compensatory deviations of the eyes designed to preserve the orientation of the visual fields and to maintain visual fixation. Clinical and experimental investigations have revealed that these deviations depend on a complex series of reflexes, some of which are still imperfectly understood. It is with the analysis of these that this paper is concerned. Before these deviations are considered, however, it is necessary to orient the reader by a general discussion of ocular movements.

The movements of the eyes are controlled by several neural mechanisms lying in the cerebral cortex and neuraxis. These mechanisms send impulses to the nuclei of the third, fourth and sixth nerves, which in turn innervate the extraocular muscles. In the terminology of Meyer, there is a simple segmental apparatus, the third, fourth and sixth nerves and their association tracts, on which certain suprasegmental structures exert a controlling influence. The latter include the oculogyric areas in the frontal lobes, areas in the occipital lobes, the cervical segments of the spinal cord and the vestibular apparatus.

VOLITIONAL MOVEMENTS OF THE EYES

In the posterior part of the second frontal convolution on either side is a small histologically differentiated area, called number 8 by Brodmann, in which volitional movements of the eyes are represented. Projection fibers pass down through the internal capsule and into the brain stem, where they form direct or indirect connections with the nuclei of the third, fourth and sixth nerves. Lesions in these cortical areas or in their projection pathways cause paralysis of conjugate movements of the eyes. In such cases, the patient may be unable to rotate the eyes upward, downward, to the right or to the left. There is

no squint and no diplopia. Moreover, a muscle which fails to act when one movement is attempted may, nevertheless, contract normally in another movement. For example, in case of loss of lateral gaze to the right, the left internal rectus muscle will fail to contract when the patient tries to look to the right but may be activated properly during convergence. Here one is dealing with loss of certain movements and not with paralysis of muscles. The same statement applies to hemiplegia and other palsies of cortical origin.

In cases of hemiplegia one finds not only loss of volitional movements but exaggeration of various reflexes. The cortical influence is believed to be twofold, including not only excitation but inhibition of the segmental structures in the spinal cord. The loss of inhibition in cases of hemiplegia results in the uncovering of reflexes which are normally obscured by cortical control. In the same way, in cases of paralysis of volitional movements of the eyes several groups of reflexes become apparent. These reflexes are, of course, present in health but are so, obscured by volitional control that they are not easy to demonstrate. Experimental and clinical investigations have shown that such reflexes arise in the retinas from visual stimuli, in the labyrinths from movements or changes in position of the head in space and in the muscles of the neck from changes in position of the head in reference to the body. Each group of reflexes will be discussed briefly. Bell's phenomenon, which is probably not a reflex but an associated movement, will also be mentioned.

OPTIC FIXATION REFLEXES [1]

The optic fixation reflexes are believed to be represented in the occipital cortex in areas adjacent to the area striata. The afferent pathway is the optic radiation, and the efferent fibers pass anteriorly through the occipital lobe medial to the optic radiation, through the internal capsule and into the brain stem, where they establish connections with the segmental oculomotor apparatus. Optic fixation reflexes are, of course, dependent on visual stimuli. Holmes [2] has pointed out that they are far more complex than simple segmental reflexes, for they require perception and imply interest and attention. It is stated that these reflexes do not develop until the third month of life.

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1. These reflexes are also termed the opticokinetic reflexes and the psychooptical reflexes.

2. Holmes, G.: The Cerebral Integration of Ocular Movements, Brit. M. J. **2:**107, 1938.

In cases in which volitional movements of the eyes are lost but the optic fixation reflexes are preserved, the following reactions may be elicited:

1. If fixation is secured on a test object and the object is then moved slowly and at a uniform rate, the patient's eyes remain directed toward the object and may be drawn into any position desired. This is termed a following movement. The same phenomenon is elicited by the revolving drum.

2. If a linear series of letters or marks is placed before the patient, it is possible for the eyes to move from letter to letter along the line until a full range of movement is secured. This is usually impossible if the letters are not placed close together.

3. If fixation is secured on a test object and the patient's head is then rotated either actively or passively, the eyes will remain directed toward the object and in this manner may be carried into any position within the orbits desired. For example, if the eyes are fixed in the primary position on a test object and the head is then rotated about a vertical axis to the right, the eyes will be carried into the position of left lateral deviation by this maneuver. According to Holmes[2] and Bielschowsky,[3] when the movement of the head is performed slowly, this reaction is entirely due to optic fixation reflexes and is abolished if fixation is prevented.

4. When volitional movements of the eyes are weak but not lost, the fixation reflex may become dominant and the patient may be forced to interrupt fixation by jerking the head or blinking the eyelids before it is possible to move the eyes. Thus, it seems that loss of volitional movements of the eyes is associated with inability to inhibit fixation reflexes.

5. The loss of optic fixation reflexes alone results in disturbances of vision, for volitional movements are not entirely sufficient for normal fixation. The eyes seem to oscillate about the object of fixation and cannot be fastened on it for more than a moment. The symptoms are more severe when the test object is moving, when the head is in movement and when the test object is placed in the peripheral fields.

6. If a test object such as a light is presented in the peripheral fields, the eyes will sometimes move toward it. This is termed an attraction movement. The relation of this movement to the foregoing reactions is not clear. Bielschowsky expressed the belief that it is merely a fully developed optic fixation reflex but admitted that there is room for difference of opinion about this interpretation.

3. Bielschowsky, A.: Lectures on the Motor Anomalies of the Eyes: III. Paralysis of Conjugate Movements of the Eyes, Arch. Ophth. **13**:569 (April) 1935.

LABYRINTHINE REFLEXES

Labyrinthine reflexes must be divided into two groups: those which arise in the semicircular canals and those which spring from the otolith apparatus.

Reflexes Arising in the Semicircular Canals.—The semicircular canals are sensory organs lying within the petrous bone and connected by way of the eighth nerve with the vestibular nuclei. Magnus [4] and his followers have shown that these structures are stimulated physiologically only by movements of the head in space or more properly by acceleration. Reflexes arising in the semicircular canals cause brief contractions of the skeletal muscles designed to maintain equilibrium during sudden movements and similar brief contractions of the extraocular muscles designed to maintain ocular fixation during movements of the head.

In cases of paralysis of voluntary movements of the eyes in which the labyrinthine reflexes are preserved, the following reactions may be elicited:

1. If the patient, seated in a Bárány chair, is rotated ten times in twenty seconds, it will be found that during the rotation the eyes are deviated in a direction opposite to that of rotation; i. e., the eyes lag behind the head. At the end of rotation, the eyes deviate in the direction of rotation and maintain this position for a short time. There is no nystagmus in such cases.

2. If the examiner takes the patient's head in his hands and twists it suddenly with a quick jerk to one side, the eyes are deviated during the movement in an opposite direction, but at the end of the movement they deviate for a short time in the direction of the movement. The reaction is, of course, identical with that just described, but the stimulus is a milder one and more truly physiologic.

3. Irrigation of one ear with cold water causes deviation of the eyes to the side of the irrigation. If the water is hot, the deviation is in the opposite direction.

4. Loss of the semicircular canal reflexes [5] in an otherwise normal subject results in loss of accurate fixation when the head is in movement. This was emphasized by Ford and Walsh [6] and confirmed by

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4. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

5. It is probable that loss of otolith reflexes also plays an important role in the symptoms due to section of the vestibular nerves.

6. Ford, F. R., and Walsh, F. B.: Clinical Observations upon the Importance of Vestibular Reflexes in Ocular Movements, Bull. Johns Hopkins Hosp. **58**:80, 1936.

Dandy [7] and Crowe [8] in a study of patients whose vestibular nerves had been sectioned. The test object seems to oscillate before the patient's eyes whenever the head is in motion, but as soon as the head is immobilized the vision becomes clear, even if the test object is in movement.

Reflexes Arising in the Otolith Apparatus.—The otolith apparatus includes the utriculus and the sacculus, which are sometimes termed collectively the static labyrinth. These structures are sensory organs the afferent fibers of which lie in the vestibular nerves and end in the vestibular nuclei in close proximity to those of the semicircular canals. Magnus and others have shown that the otolith organs are stimulated under physiologic conditions by changes of the position of the head in space. The stimulus is apparently the weight of the otoliths. Reflexes arising in these organs cause tonic, sustained contractions of skeletal muscles, which produce changes in posture. The altered posture is preserved as long as the new position of the head is maintained. As regards the eyes, the otolith reflexes produce tonic deviations and rotations of such a type as to compensate for the change in position of the head and to preserve as far as possible the normal orientation of the visual fields. McNally and Tait,[9] who have made important contributions in this field, stated that the sacculus has no demonstrable connection with postural reactions and that the aforementioned reflexes are all derived from the utriculus. Despite a number of investigations, the importance of the otolith reflexes in man is still uncertain. The following reactions, however, are described:

1. When the head is placed in a position of flexion, the eyes show upward tonic deviation. When the head is held in extension, the eyes are deviated downward.

2. When the head is placed in a position of inclination to either shoulder, the eyes are rotated on the visual axis in the opposite direction in such a way as to compensate for the altered position of the head and preserve their previous orientation. Fischer's [10] studies are the most recent of many.

7. Dandy, W. E.: Ménière's Disease: Symptoms, Objective Findings and Treatment in Forty-Two Cases, Arch. Otolaryng. **20**:1 (July) 1934.

8. Crowe, S.: Ménière's Disease: Study Based upon Examinations Made Before and After Intracranial Division of the Vestibular Nerve, Medicine **17**:1, 1938.

9. McNally, W. J., and Tait, J.: Some Features of the Action of the Utricular Maculae and of the Associated Action of the Semicircular Canals of the Frog, Phil. Tr. Roy. Soc., London **224**:241, 1934.

10. Fischer, M. H.: Messende Untersuchungen über die Gegenrollung der Augen und die Lokalisation der scheinbaren Vertikalen bei seitlicher Neigung des Kopfes, des Stammes und des Gesamtkörpers, Arch. f. Ophth. **118**:633, 1927.

3. Changes of position of the head produced by rotation about a vertical axis produce no otolith reflexes, for the position of the head in the field of gravity is not altered.

TONIC NECK REFLEXES

Magnus [4] has shown that in experimental animals changes in the position of the head in relation to the body cause, among other postural reactions, tonic deviations and rotations of the eyes. These reactions are compensatory and of the same nature and direction as the otolith reflexes. They are produced by afferent impulses derived from the muscles of the neck and are abolished if the cervical nerve roots are sectioned. There is little evidence that such reflexes are important in man. Fischer [10] has estimated that in normal subjects movements of the body with the head fixed in an upright position cause at most ocular deviations of not more than 2 or 3 degrees. Such reactions cannot play an important role, therefore, among the phenomena with which this paper deals.

BELL'S PHENOMENON

In cases in which conjugate upward movements of the eyes are lost as a result of a supranuclear lesion, it is well known that strong efforts to close the eyelids against resistance will result in the eyes being rolled up involuntarily. The same reaction is found in normal subjects and is always evident in cases of paralysis of the seventh nerve. This is called Bell's phenomenon. It is evidently an associated movement constituting a part of the act of closing the eyelids. It is probable that the movement of the bulbs arises in cortical areas in which movements of the lid are represented and not in the oculogyric areas. It would seem, therefore, that this phenomenon has no significance as regards the state of the oculomotor system except that of indicating that the third nerves are intact.

REPORT OF CASES

As the title of this paper indicates, we are particularly concerned with the analysis of the deviations of the eyes produced by movements, or changes in positions, of the head. We shall present 2 cases in which these deviations were demonstrable. The first case illustrates only well known reactions which have been repeatedly described by Holmes, Bielschowsky and others. It is given merely for contrast with the second case, which is an unusual one and of considerable theoretic importance.

CASE 1.—*Disseminated sclerosis associated with loss of voluntary lateral move-* •
ments of the eyes in a man aged 25; deviations to right or left produced by movements of the head.

In A. M., a previously healthy man of 25 years, difficulty in gait and disturbances of vision developed. Neurologic examination revealed unsteady station and gait, ataxia of the cerebellar type in both arms and legs, scanning speech, loss of abdominal reflexes and bilateral extensor plantar responses. A diagnosis of disseminated sclerosis was made. The following reactions were elicited in the examination of the eyes:

1. Vision was 20/15 in each eye, and the fields were of normal outline. The pupils reacted well to light and during accommodation, and the optic disks showed no pathologic changes.

2. The movements of the eyes in the vertical·plane were of full range.

3. It was impossible for the patient to deviate his eyes to the left of the midline when they were kept open. By blinking his eyelids or jerking his head, however, he could carry his eyes through almost a full range of movement to the left. It was found that the blinking or jerking of the head was designed to interrupt fixation, for when one or both eyes were closed the movement of the eyes to the left was greatly facilitated. When his eyes were in left lateral deviation, he would blink and the eyes would return to the primary position.

4. It was possible for the patient to deviate his eyes about 10 degrees to the right with both eyes open, but if fixation was interrupted he could move them into the extreme lateral position.

5. When the patient was instructed to fix a test object which was then moved slowly to one side or the other, the eyes would follow into the right or the left lateral position.

6. When the eyes were fixed on a test object and the head was rotated slowly to the right or left, the eyes would remain fixed on the object despite the movement of the head, so they could be carried into the extreme lateral position within the orbits. This reaction was abolished when fixation was prevented.

7. When the head was turned suddenly with a quick jerk by the examiner, the eyes could be carried to either side even when fixation was prevented, but this reaction was poorly sustained and the eyes flickered back to the primary position almost at once.

8. Caloric irrigation of either ear produced full deviation of the eyes to either side, and rotation in a Bárány chair produced the same result.

CASE 2.[11]—*Congenital double athetosis associated with congenital paralysis of upward and downward movements of the eyes in a boy 13 years of age; elevation and depression of eyes in the orbits by active and passive movements of the head.*

L. S., a boy of 13 years, was examined on June 15, 1939. Neurologic examination revealed the usual signs of double athetosis, which was known to be stationary and which had been noted early in childhood. It had never been possible for the child to make satisfactory progress in learning to read despite the fact that his intelligence seemed to be normal. His teachers stated that the difficulty seemed to lie in his inability to move his eyes properly. Examination of the eyes gave the following information:

1. Vision and the visual fields were normal. The pupillary reactions were brisk. The optic fundi were normal.

2. Voluntary movements of the eyes to the right and left were normal. The patient could follow a moving object with his eyes to either side.

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11. This patient was examined at the Children's Rehabilitation Institute of Baltimore, by the courtesy of Dr. Winthrop Phelps and Mr. B. M. Wapole.

3. Voluntary movements of the eyes downward below the horizontal were absent. When fixation was prevented by closing the eyes, there was still no downward movement.

4. Voluntary movement of the eyes upward was difficult and limited to less than 10 degrees.

5. Convergence was entirely absent.

6. It was impossible for the patient to follow a test object moving slowly in the vertical plane. This test was made repeatedly. The revolving drum failed to produce any reaction when it was revolved about a horizontal axis.

7. When the patient's head was extended actively or passively, compensatory deviation of the eyes downward occurred. By this means the eyes might be rotated to the limit of their normal excursion. In the same way, flexion of the head caused upward deviation of the eyes. These reactions were secured just as easily when the eyes were closed as when they were open and by slow movements of the head as well as by rapid movements. They were quite constant and never varied in the slightest degree.

8. The patient was placed on a tilting table in such a manner that no movement of the neck could occur. When he was rotated from an upright position backward, his eyes deviated downward just as when his head was extended on the body. When he was rotated from a horizontal to a vertical position, his eyes deviated upward just as when his head was flexed on the body. It was clear that it was the change in the position of the head in space and not any movement of the head on the body that caused the deviations of the eyes. The ocular deviations were all well sustained.

9. The patient had learned an interesting trick by which he could deviate his eyes downward. When asked to look at an object in his lap, he would flex his head and the upper part of his trunk as strongly as possible. During this movement his eyes were of course rotated upward in the orbit, but by extreme flexion of the spine he could finally bring them to bear on the test object, for the range of movement of his head was greater than that of his eyes. At this point he would bring his head up into the upright position and his eyes would remain fixed on the test object in a position of downward deviation. The examiner could reproduce this reaction by making passive movements of the patient's head. It was also possible to fix the patient's eyes on an object above his head by making extreme extension of the head and then bringing it to an upright position. The patient failed to discover the latter maneuver until the examiner demonstrated it to him.

10. Bell's phenomenon was present; that is, if the patient's eyelids were held open and the patient was requested to try to force them together, the eyes would roll up.

COMMENT

In the first case, in which there was loss of volitional lateral movements of the eyes, two types of compensatory deviations were demonstrated: 1. Deviations produced by slow rotation of the head to left or right during fixation of a test object. These reactions were abolished if fixation were prevented. It seems to be generally agreed that these reactions are due to optic fixation reflexes, and we have no reason to disagree. When the head is in the upright position, this maneuver cannot stimulate the otolith organs. 2. Deviations produced

Fig. 1 (case 2).—Volitional movements of the eyes. *A* shows full range of movement to the right, and *B*, full range of movement to the left.

Fig. 2 (case 2).—Deviations due to movements of the head. *A* shows deviation of the eyes downward when the head is passively extended, and *B*, deviation upward when the head is flexed.

Fig. 3 (case 2).—Reactions on the tilting table. *A* shows upward deviation of the eyes due to bringing the patient from a horizontal to an upright position. *B* shows downward deviation of the eyes due to rotating the patient from an upright position backward to a horizontal position.

by rotation of the head to right or left by means of a quick jerk. These deviations were poorly sustained and might be produced even when fixation was prevented. There is no apparent reason to dispute Bielschowsky's statement that these reflexes are due to stimulation of the semicircular canals.

In the second case there was loss of voluntary movements of the eyes in the vertical plane. When the head was actively or passively flexed or extended, the eyes deviated upward or downward, respectively. These movements were of full range, and the deviation of the eyes was maintained as long as the head was held in the altered position. Slow movements were just as effective as rapid ones. The same reactions were elicited when the eyes were closed. It is obvious that these reactions are different from those described in the first case and that they require further discussion. Four possibilities should be considered: optic fixation reflexes, tonic neck reflexes, semicircular canal reflexes and otolith reflexes.

The fact that the reactions described could be elicited with the eyes closed would seem to rule out the possibility of optic fixation reflexes. Moreover, the patient could not follow with his eyes an object moving slowly in the vertical plane, and there was no reaction to a revolving drum when it was rotated about a horizontal axis. The patient, therefore, seemed to have lost all optic fixation reflexes in the vertical plane.

Since the reactions described were elicited when the patient was fastened on a tilting table in such a way as to prevent any movement of the neck, it would seem evident that the tonic neck reflexes played no important role. If Fischer's measurements are correct, the tonic neck reflexes are of small amplitude and at most could only augment these reactions to a minor degree.

Against the possibility that the semicircular canal reflexes were responsible is the fact that slow movements were just as effective as rapid ones and that deviations were tonic and were sustained as long as the altered position of the head was maintained. Reflexes arising in the semicircular canals are of brief duration and phasic rather than tonic.

We are inclined to believe, therefore, that these reactions are due to otolith reflexes. They are produced by altered position of the head in space just as otolith reactions are; they are in the same direction as the otolith reactions, and they are well sustained tonic deviations just as the otolith reactions are known to be. Moreover, we have presented evidence to show that they cannot be attributed to reflexes arising in the retinas, the semicircular canals or the muscles of the neck.

Little can be said about the site of the anatomic lesions. In the first case, which was one of disseminated sclerosis, one must assume

that bilateral plaques had interrupted the projection fibers of the frontal lobes which control lateral gaze and that fibers derived from the occipital cortex and the vestibular apparatus remained intact. Such lesions might be found in the pons. In the second case we were apparently dealing with a defect of development, which, as regards movements in the vertical plane at least, had destroyed almost all cortical influence on the eyes but had not affected the vestibular apparatus. One might expect to find the lesion in the upper part of the midbrain.

SUMMARY AND CONCLUSIONS

We have given a brief discussion of the clinical phenomena found in cases of paralysis of volitional ocular movements and of the various reflexes which are uncovered in this condition. We have described the reflexes which arise in the retinas, the semicircular canals, the otolith organs and the neck.

A case of loss of lateral gaze is described in which the eyes might be moved laterally by active and passive movements of the head. The ocular deviations were of two types: (*a*) those produced by slow movements of the head, which were well sustained and were abolished if fixation were prevented, and (*b*) those produced by sudden, quick movements of the head, which were poorly sustained and which persisted when fixation was prevented. We believe the first type of deviations to be due to optic fixation reflexes and the second type to reflexes arising in the semicircular canals.

A more remarkable case is also presented in which volitional movements of the eyes in the vertical plane were lost. When the head was flexed the eyes deviated upward, and when the head was extended the eyes deviated down. These deviations were well sustained and were not dependent on fixation. Slow movements were as effective as quick movements. By the use of the tilting table, it was shown that these reactions were not due to tonic neck reflexes. We believe that they arose in the otolith organs. These observations suggest that in man as well as in experimental animals the otolith reflexes play an important role in the tonic deviations of the eyes which are associated with movements of the head.

CHOROIDEREMIA

BENJAMIN FRIEDMAN, M.D.
NEW YORK

Reports of cases of choroideremia are still sufficiently rare to warrant the publication of an additional one. As the name implies, choroideremia is characterized by an almost total absence of choroid. The fundus picture is striking. A glaring white or greenish white sheen is reflected from the interior of the eye. One sees the almost naked sclera, made evident by the defection of the choroid and the pigment epithelium of the retina. In the macular region alone is the normal reddish coloration retained; here an island of choroidal circulation bravely withstands the surrounding dissolution, with the end that central vision is preserved. A few attenuated remnants of the choroidal vascular system are to be seen; these run a straight and lonely course. Here and there small stellate or cuneiform clumps of pigment are found in the retinal strata. The retinal circulation is unimpaired, although the vessels are somewhat thinner than normal. The disks are normal in appearance. Cataractous changes do not occur in the lens. The clinical manifestations of the disease are reminiscent of retinitis pigmentosa—night blindness and extreme contraction concentrically of the visual fields, particularly for color. The central acuity of vision remains surprisingly unaffected. The condition is bilateral, occurs (with one exception) in males and is associated with myopia.

REPORT OF A CASE

D. S., white, aged 45, presented himself at the Knapp Memorial Eye Hospital for a routine examination.[1] He stated that his vision at night had been poor all his life. An uncle, now deceased, had also suffered from night blindness, but two brothers and two sisters were apparently normal. The patient is not deaf, and he has no supernumerary digits or other congenital aberrations. His hair is entirely gray and has been so since the age of 20.

The patient complained that his vision had depreciated during the past year; further questioning revealed that this reference concerned central vision. This was reestablished to its previous level by new lenses. His night blindness had always been marked, especially since the age of 13 or 14 years, but had not become more disabling since that time.

The vision in the right eye was 20/30 + with a — 6.50 D. sph. ⌒ — 1.00 D. cyl., axis 180; that of the left eye was 20/50 — when corrected with a — 6.50 D. sph. ⌒ — .50 cyl., axis 75.

The Wassermann test was negative.

Ophthalmoscopic examination disclosed in each eye the characteristic absence of choroid over the entire fundus with the exception of an island in the macular region. Another small crescentic remnant of choroid persisted just temporal to the disk, and from this a fairly thick artery extended to the macula and anastomosed with the vessels at that site. These two almost desiccated patches served as the fountainhead of what little choroidal circulation still survived. From these emerged perhaps a dozen extremely narrow arteries which ran either upward or downward and gradually thinned out into nothingness. They did not extend beyond half way to the ora serrata. They did not give off any tributaries or effect any anastomoses. About 2 disk diameters above the macula a vessel perforated the sclera, and after making an umbrella handle bend it ran off ineffectually in a vertical direction.

The retinal circulation was excellent; the arteries were only slightly thinned, and the disk was of a normal pink appearance. A small amount of pigment was scattered over the fundus in the forms of circular, stellate or cuneiform clumps. These deposits were not particularly related to the blood vessels.

The visual fields were contracted, in the right eye to the 15 degree circle and in the left eye to the 10 degree circle. Color recognition was confined to the very center.

The patient was treated with several series of injections of sodium nitrite to which an inorganic salt had been added (nitroscleran) supplemented with the administration of erythrityltetranitrate. Subjectively, there seemed to be an improvement, but this could not be substantiated by an objective demonstration of improvement in the visual field or an increase in the visual acuity.

COMMENT

Choroideremia, as has been indicated, has certain characteristics in common with retinitis pigmentosa—night blindness and concentrically contracted fields. It has been thought to represent a form of retinitis pigmentosa. There are other points, however, wherein the two conditions differ. The rarity of choroideremia and the frequency of retinitis pigmentosa do not point to a common origin. Choroideremia, judging by most of the recorded histories, seems to affect its victims almost as profoundly early in life as later on; that is to say, the patients do not complain of disability increasing over a long period. This is in contrast to the relentlessly progressive nature of retinitis pigmentosa and would indicate an early end point in its pathologic status. The waxy appearance of the disks, the extreme narrowing of the retinal arteries and the posterior cortical cataracts which are found in retinitis pigmentosa are not noted in choroideremia. Retinitis pigmentosa is often accompanied by degeneration of the macula; in choroideremia the macula is conspicuously salvaged. The central visual acuity continues to deteriorate in retinitis pigmentosa, but in choroideremia it seems not to be greatly depressed.

Bedell [2] has carefully reviewed the known cases, some 20 authentic instances, with several questionable ones. It is a tribute to the clinical

2. Bedell, A. J.: Choroideremia, Arch. Ophth. **17**:441 (March) 1937.
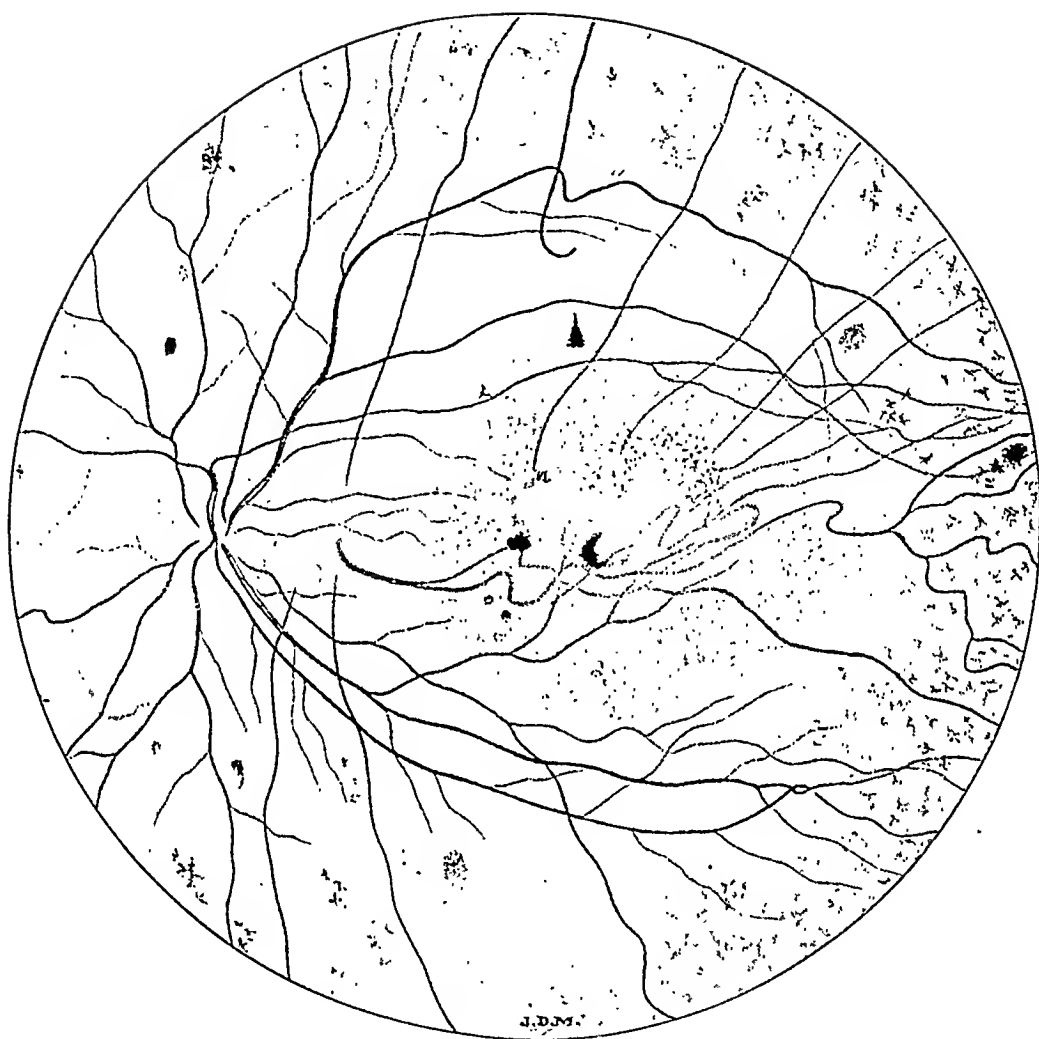
Choroideremia.

experience of Dr. Bedell that he was able to add 5 cases from his own practice. Too little is known of the disease to warrant more than a conjecture as to its causation. Bedell stated that "as it develops during the life of the patient it is not to be considered as a congenital absence of the choroid, but as a dissolution of that membrane."

The earliest case on record is that of Bhaduri,[3] who reported the condition in a Hindu boy of 17. The father stated that he had been aware of his son's ocular trouble since the boy was 3 years of age.

In speaking of primary choroideremia (as distinguished from partial loss of the choroid due to secondary atrophy in retinitis pigmentosa and gyrate atrophy of Fuchs), Ida Mann[4] remarked:

The sporadic ones are possibly purely developmental, the chorio-capillaries having failed to form, not having disappeared secondarily. The absence may be complete (very rare), or partial when it is present at the posterior pole and absent in the equator, sometimes in a ring, sometimes right to the periphery. Smaller localized patches of absence would be obviously included under atypical colobomata. The genesis of the condition may involve one of two mechanisms. Either most or all of the ciliary arteries (short posterior and anterior) may fail to bud out from the ophthalmic artery at the 16 mm. stage, or the outer layer of the optic cup may fail to produce pigment (at the 10 mm. stage) and so the stimulus for the capillary growth may fail, even though the arteries do bud out.

The first is the possible cause of those cases in which even the larger vessels of the choroid cannot be seen, while the latter is likely in the cases where patches of normal chorio-capillaries are present.

On the whole, the question of the occurrence of primary choroideremia is not yet understood, owing partly to its rarity, partly to the absence of microscopic examination and partly to the lack of examination of affected individuals in earliest infancy, so that it is never possible to say whether a case is truly congenital or has arisen as an infantile degeneration which would merely class it as a sporadic case of the abiotrophic group.

It seems odd, however, to fail to note the other congenital deformities which not infrequently accompany congenital abnormalities of the fundus. For instance, colobomas of the lens, iris or nerve head are not seen in connection with choroideremia, nor is nystagmus to be observed. It seems also difficult to explain on a congenital basis why the macula, which is so often the seat of dysplasia, should be so consistently exempted in these cases.

The problems of origin and causation can be settled only by earlier and more careful examinations of the fundi in families giving a history of night blindness in a member, followed by years of subsequent observation and by microscopic studies. The latter have so far not been available, but it is to be hoped that greater familiarity with the disease will encourage more enlightening clinical investigations and possibly lead to opportunity for histologic analysis.

3. Bhaduri, B. N.: Choroideremia, Calcutta M. J. **28**:428 (April) 1934.
4. Mann, I.: Developmental Abnormalities of the Eye, New York, The Macmillan Company, 1937, p. 196.

Ophthalmologic Reviews

PULSATING EXOPHTHALMOS

H. SAUL SUGAR, M.D.

AND

SAMUEL J. MEYER, M.D.

CHICAGO

Since the first clinical description of the condition known as pulsating exophthalmos by Travers in 1809, there have been 621 cases collected up to 1927. Because cases of this type are comparatively rare and because each author has usually seen only one or two cases of his own, there has been a great diversity of opinion as to their management. Wheeler in 1934 stated that "in the main, the handling of pulsating exophthalmos has been the discredit of the medical profession because methods have not been worked out in advance and the subect has not had careful thought by most surgeons. The principles involved in the surgical relief of pulsating exophthalmos should be in the minds of ophthalmologists." Harkness expressed the belief that "a condition of such rarity and with such striking symptomology is deserving of record whenever encountered."

We have reviewed the literature since Harkness' report, bringing the total cases of pulsating exophthalmos to 786 (to 1939) and have added 6 of our own, 3 of which were seen within a period of three months at the Illinois Eye and Ear Infirmary. The pulsating exophthalmos in 3 of the 6 cases was due to a carotid-cavernous aneurysm, in 1 to an orbital arteriovenous aneurysm and in 1 to an orbital angioma. The postmortem observations in 1 of the cases of carotid-cavernous aneurysm are recorded.

Travers, in addition to describing the disease entity, devised the operation of ligation of the common carotid artery. The first pathologic study to test Travers' views was made by Guthrie in 1823. He found an aneurysm of the ophthalmic artery. This was accepted as the cause of pulsating exophthalmos until it was shown by Baron in 1835 that in the usual case the exophthalmos might also be due to an intracranial arteriovenous communication. In 1851 Brainard, professor of surgery at Rush Medical School, cured a patient with pulsating exophthalmos

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by causing thrombosis of the orbital venous varices by the introduction of hot needles into them. France in 1855 reported the first spontaneous cure. Three years later Gioppi, of Padua, recommended digital compression. The following year, in 1869 Buck reported bilateral ligation of the carotid arteries in 1 case. In 1874 Lansdown cured a patient with pulsating exophthalmos due to trauma by ligating the branches of the superior ophthalmic vein at the inner canthus of the eye. This method is still widely used by the Russian surgeons. Murray in 1904 first successfully ligated the internal carotid artery.

In 1880 a report of 106 cases was made by H. Sattler. Keller and Reuchlin reported 138 cases in 1898 and 1902, respectively. De Schweinitz and Holloway in their monograph in 1908 reported 69 cases. Eighty-eight more were gathered by Bedell (1915), Rhodes (1916), Zentmayer (1916) and von Nagy (1919). C. H. Sattler in 1920 reported on a group of 322 cases. Locke in his excellent paper reported 131 cases in 1924.

In 1930, Harkness brought the total to 621 up to 1927. King in 1931, Loos and Irsigler in 1932 and Hahn in 1938 reported smaller incomplete groups of cases.

Of the several anatomic causes of pulsating exophthalmos, the most frequent is traumatic rupture of the internal carotid artery in its passage through the cavernous sinus. Rawlings stated that 70 per cent of fractures of the base of the skull involve the body of the sphenoid bone. Both the internal carotid artery and the cavernous sinus are comparatively immobile in this region; so the underlying fracture may rupture or injure their walls. Penetrating wounds may also rupture or weaken the arterial walls. Next most frequent as a cause of this condition is a spontaneous arteriovenous fistula between the internal carotid artery and the cavernous sinus, most frequently due to generalized arteriosclerosis. Syphilis has occasionally been a predisposing factor by causing sclerosis of the walls of the carotid artery. Other causes are vascular tumors of the orbit or surrounding structures, simple aneurysm of the ophthalmic artery, simple aneurysm of the extracavernous portion of the internal carotid artery, arteriovenous communication between the internal carotid artery and the internal jugular vein at the entrance of the carotid canal, arteriovenous communication in the orbit and absence of a large part of the orbital roof.

Wheeler has classified pulsating exophthalmos due to absence of the orbital roof into three groups: (a) that due to congenital absence of the orbital roof, (b) that due to absence of the roof as an accompaniment of plexiform neurofibroma and (c) that due to surgical removal of the orbital roof. A fourth group, that due to traumatic bony dehiscences, with or without herniation of the brain, might be added to Wheeler's classification. Baron and Frauendorfer reported cases of this type.

One case of pulsating exophthalmos due to arteriovenous aneurysm in the neck has been reported by Terry and Mysel. O'Shea reported a case in which a mucocele of the sphenoid sinus was the contributing cause and Jaensch 1 in which it was an encephalocele.

These cases in which the syndrome of oculo-orbital pulsation is present are best divided into two groups as follows: (1) true pulsating exophthalmos, including (*a*) carotid-cavernous aneurysm, (*b*) intraorbital aneurysm, either arteriovenous or of the ophthalmic artery, rarely (*c*) arteriovenous aneurysm between the internal carotid artery and the internal jugular vein at the entrance into the carotid canal and (*d*) simple aneurysm of the internal carotid artery; (2) false, or pseudo-, pulsating exophthalmos, including orbital angioma, meningocele and absence of a large part of the orbital bony roof.

In the 165 cases gathered by us, excluding our own, the exophthalmos in 143 may be classified as true pulsating exophthalmos and in 19 as the pseudo pulsating type; the type was not mentioned in 3 cases. In 131 of the 143 cases the exophthalmos was due to carotid-cavernous aneurysm, in 8 to an orbital aneurysm or arteriovenous communication, in 3 to an intracranial aneurysm and in 1 to an arteriovenous communication in the neck. The false pulsating exophthalmos in 14 of the 19 cases was due to destruction of an orbital wall, in 3 to orbital tumor, in 1 to mucocele and in 1 to encephalocele. In 1 of the cases with a defect in the orbital wall varices of the nasal mucous membrane were present which caused intermittent pulsating exophthalmos.

Pregnancy may be an element in the vascular type of pulsating exophthalmos. Terry and Fred reported a case of spontaneous communication between the angular vein and the infratrochlear branch of the ophthalmic artery in the latter part of pregnancy.

In studying the etiologic factors in 544 cases in which the factors were stated, Locke found that the exophthalmos in 126 (23.16 per cent) was spontaneous and in 418 (78.84 per cent) traumatic in origin. The exophthalmos of spontaneous origin was due to intraorbital tumor in 25 per cent of cases, to simple aneurysm in 25 per cent and to arteriosclerosis in 50 per cent. In our series of 110 cases of exophthalmos of stated vascular type, the causative factor was traumatic in 83 and spontaneous in 27.

Locke found the average age of patients with pulsating exophthalmos of spontaneous origin to be near the end of the fifth decade. We found the average age in our group to be 44.2 years. Among the patients with pulsating exophthalmos of traumatic origin, Locke found the average age to be near the end of the third decade. We found it to be 36.4 years. Only cases of exophthalmos of the vascular type are considered.

In Locke's group of cases of pulsating exophthalmos of traumatic origin, males predominated 3 to 1 (76.76 per cent). In our group, males likewise predominated 2.2 to 1 (53 males to 25 females). In Locke's group of cases of pulsating exophthalmos of spontaneous origin, females predominated (74.13 per cent). In our series the proportions were practically equal (14 females to 13 males).

Up to 1924, 50 postmortem examinations had been reported. These were gathered by Locke. In 33 of the cases the causative factor was spontaneous and in 17 traumatic. In 4 of the former no lesion was found. In 2 a cure had been effected, while in 1 the examination had been incomplete. In the remaining 30 cases in which the origin was spontaneous there was a communication between the internal carotid artery and cavernous sinus in 16 (53.3 per cent), an orbital tumor in 7 (23.3 per cent), an aneurysm of the internal carotid artery in 3 (10 per cent), an aneurysm of the ophthalmic artery in 3 (10 per cent) and absence of a lesion in 1 case. In the group of 17 cases in which the origin was traumatic, an arteriovenous communication between the internal carotid artery and the cavernous sinus was found in 16 (94.12 per cent) and an aneurysm of the internal carotid artery in 1 case. Since 1924 King, Ehlers, Pichini and Ellison each have reported autopsy observations in cases with carotid-cavernous fistula. Hanna reported findings in a case in which the pathologic examination of the ligated internal carotid artery showed no lesion. This case was probably one of orbital arteriovenous communication.

MECHANISM OF ORIGIN OF TRUE PULSATING EXOPHTHALMOS

After rupture of the internal carotid artery there is an overflow of arterial blood into the venous sinus with consequent increase in the venous pressure and reversal of venous flow in the ophthalmic veins and their tributaries. The resulting stasis, edema and increase in blood volume in the venous bed produce exophthalmos. Through the dilated venous channels the arterial pulsation is transmitted to the eyeball and orbital tissues. Since the ophthalmic veins are the only tributaries of the cavernous sinus which have no dense tissues around them, such as is present around the intracranial venous sinuses, they may dilate and give rise to the pulsating large venous masses often seen at the internal angle of the eye, usually consisting of the superior ophthalmic vein formed by the union of the supraorbital and angular veins. The pulsation may be limited, rarely, to the venous masses.

In the cases in which the exophthalmos was of spontaneous origin it is believed that weakening of the vessel walls or rupture of simple aneurysms are the chief direct causes of the arteriovenous fistula.

Of the rare cases of pulsating exophthalmos in which the condition becomes bilateral, de Schweinitz stated: "Following the venous disten-

tion on one side there is an extension of the process by the transverse and circular sinus to the venous channels of the opposite side." Terry and Mysel suggested that another explanation for the bilaterality is an unusually wide communication between the paired sinuses. In one of our cases in which the second eye became involved while the patient was under observation and in which autopsy was later performed, the fistula was present only on the side of the greater exophthalmos. Examination of the fundi during life showed the vessels of the second eye to be normal, while those of the first eye were markedly dilated and tortuous.

CLINICAL PICTURE OF PULSATING EXOPHTHALMOS DUE TO CAROTID-CAVERNOUS ANEURYSM

The most frequent history is that after a severe trauma there is a period of unconsciousness, on recovery from which there is a swishing noise in the head, often failure of vision and unilateral exophthalmos. The exophthalmos may occur simultaneously with the bruit but more frequently follows it. Vertigo may be an annoying symptom in some cases. All symptoms usually tend to be exaggerated by stooping and by any physical exertion.

Objectively, pulsating exophthalmos is characterized by proptosis of one, or rarely, both eyeballs. There frequently is a loss of motility of the globe in one or more directions, most frequently laterally. Palpation of the lid-covered globe reveals a thrill. It may be necessary to apply slight pressure to the globe to elicit pulsation, which may or may not be obvious. The stethoscope reveals a swishing bruit synchronous with the radial pulse, diminishing or disappearing with pressure over the common carotid artery in the neck on the involved side. There is often a marked swelling of the lids and chemosis of the conjunctiva, especially the lower palpebral portion, which may evert the tarsal portion of the lower lid. The bulbar conjunctiva may reveal a Medusa-head-like engorgement and tortuosity of the veins. The cornea may be affected by lagophthalmos. The arteries and veins of the retina are almost constantly engorged and tortuous. In a case reported by Kattan the condition had been present for twenty-five years, yet the central vein was normal. Kattan explained this by the assumption that the central vein may pour its blood into the inferior ophthalmic vein instead of the superior; hence the blood may pass to the pterygoid plexus and not reach the cavernous sinus. Edema of the disk margins, retinal hemorrhages, clouding of the vitreous or atrophy of the optic nerve may be found. Venous masses at the inner canthus may occur. The lesions tend to be progressive, although some have cleared up spontaneously.

The first eight cranial nerves, especially the sixth, may be involved by the direct effects of the original trauma, by the direct pres-

sure of the dilated vessel, by hemorrhage or by the venous congestion and stretching due to the exophthalmos. The supraorbital nerve alone may be involved by pressure by the pulsating superior ophthalmic vein and its tributaries at the exit of the nerve from its canal.

According to de Schweinitz, 20 per cent of all cases terminate in blindness, and in no more than 11.1 per cent is normal vision retained.

GLAUCOMA IN CASES OF PULSATING EXOPHTHALMOS

Hudelo in 1928 classified pulsating exophthalmos in the group of causes of secondary glaucoma together with other conditions in which venous stasis was present. This group consists of thrombosis of the central retinal vein, cyanosis retinae, thrombosis of the cavernous sinus and facial angioma in addition to pulsating exophthalmos. He cited the changing proportion of cases in which glaucoma was found since the clinical entity of pulsating exophthalmos was recognized. Before 1880 H. Sattler found 4 cases of glaucoma in 106 cases of pulsating exophthalmos, a proportion of 1 to 26. Between 1880 and 1902, 14 cases were recorded in a total of 138, a proportion of 1 to 10. C. H. Sattler found a proportion of 1 to 8 in 108 cases. Hudelo found 16 cases of glaucoma in 64 collected cases from 1919 to 1928, a proportion of 1 to 4. In the cases gathered by us from 1927 through 1938, only 11 definite cases of glaucoma were found. These include the cases of D. and E. Lazarescu, Dandy, Blumenthal, Baurmann, Dupuy-Dutemps, Hanford and Wheeler, Kattan, Valière-Vialeix and our cases. In 1 of our cases the tension did not rise above 35 mm. of mercury (Schiötz) and was unaffected by miotics. In 3 of our other cases the tension in the exophthalmic eye was higher than in the opposite eye. In the case reported by Hanford and Wheeler, acute glaucoma occurred after bilateral ligation of the common carotid artery. In Dandy's case glaucoma and cataract developed after ligation of the internal and common carotid arteries.

The fact that a large number of the reported cases were from general surgeons and neurosurgeons may explain the smaller percentage of glaucoma in our collected cases. In many of the cases apparently no attention was paid to the intraocular tension.

DIAGNOSIS

In order to obtain accurate localization of the site of the lesion, several corroborative laboratory tests have been made. Terry and Mysel used 25 cc. of thorium dioxide intra-arterially in 1 case and obtained roentgen evidence of an arteriovenous fistula between the internal carotid artery and the internal jugular vein in the neck. This method was attempted unsuccessfully twice in 1 of our cases.

Pichini used potassium iodide successfully in angioencephalography to diagnose a carotid-cavernous fistula. S. W. Gross used 35 per cent diodrast.

Brown used chemical determinations of the oxygen content of the blood of the regional veins to make a diagnosis of arteriovenous aneurysm. He collected samples under oil and used the Van Slyke gasometric method of analysis. He mentioned Branham's sign, a sharp slowing of the pulse with closure of the fistula by compression of the arterial vessel in the neck, as a further aid.

Baurmann suggested a dynamometric method of diagnosis. In a case of pulsating exophthalmos due to carotid-cavernous fistula he found an increase of pressure in the central vein on the affected side from 49 to 61 mm. of mercury by digital compression of the common carotid artery (which incidentally causes compression of the internal jugular vein). The diastolic pressure in the involved central artery fell from 62 to 56 mm. of mercury as would be expected normally. Baurmann expressed the belief that the venous pressure increased because of continued flow of blood from the circle of Willis of the opposite side through the fistula into the cavernous sinus. The arterial pressure fell somewhat because blood could flow out to some extent through anastomoses between the middle meningeal artery and the ophthalmic artery. In this particular case a spontaneous cure took place clinically. Dynamometric studies, however, revealed that the opposite arteries had taken over the function of the carotid artery on the affected side. Normally pressure on the carotid artery causes an increase in pressure on the opposite side and a decrease on the same side. However, in this case compression of the common carotid artery on the affected side caused the pressure in the central artery on the same side to sink only a few millimeters but did not affect that on the other side. Pressure on the common carotid artery on the unaffected side caused a marked decrease in pressure, associated with collapse. Baumann expressed the belief that the dynamometer could thus be used as a test of function of the carotid artery.

In attempting to make an etiologic diagnosis of the various types of pulsating exophthalmos, a history of trauma, the presence of pulsation over the inner canthus and a bruit, especially a loud one, are usually indicative of the type due to an arteriovenous fistula. A bruit may rarely, however, occur in noncommunicating aneurysms. The latter are more apt to occur in middle-aged and elderly persons.

According to de Schweinitz, pulsating exophthalmos due to an orbital tumor develops slowly. The bruit is feeble if present at all.

The pulsation due to defects of the orbital roof or to orbital encephalocele is transmitted from the brain. There is no bruit. The pulsation is easily seen, and there is no dilatation of the veins of the eyeball.

Exophthalmos due to disease of the nasal accessory sinuses does not usually manifest any bruit or pulsation. Varices of the nasal mucosa in the presence of a defect of the nasal wall of the orbit may, however, cause intermittent pulsating exophthalmos, as evidenced by a case reported by De-Petri.

REPORT OF CASES

Group 1: True Pulsating Exophthalmos Due to a Carotid-Cavernous Communication.—CASE 1.—L. H., a 71 year old white woman, presented herself at the Illinois Eye and Ear Infirmary, service of Dr. L. Hoffman, on Nov. 20, 1938. She had awakened one morning five weeks earlier with a peculiar pounding sensation in her head. There was no paralysis or weakness. The pounding noise continued. Two weeks later the right upper lid began to droop, and both right lids became swollen. The noise in the head and swelling persisted. There had been no trauma of any kind.

Vision in the right eye was 20/200 uncorrected. It could not be improved with lenses. Vision in the left eye was 20/200; it was corrected to 20/70 with a —3.00 D. cyl., axis 180. Tension was 25 mm. of mercury in the right eye and 18 mm. in the left eye. (Schiötz, corrected values according to Friedenwald.)

External examination of the right eye showed the eye to be obviously proptosed. Exophthalmometer readings (Hertel) were 27 mm. for the right eye and 17 mm. for the left eye (at 100 mm.). The upper lid was ptosed and immobile. The palpebral fissure was 2 mm. wide, compared to 11 mm. on the left, when the patient looked upward. The veins of the upper lid were markedly engorged. The lower lid was completely everted by a markedly chemotic palpebral conjunctiva. The globe was immobile and held in the primary position. Palpation of the globe through the upper lid revealed a thrill and pulsation synchronous with the radial pulse. The bulbar conjunctiva was somewhat chemotic, with dilated, tortuous episcleral veins. There was a horizontal band of epithelial opacity, 1.5 by 8 mm., in the interpalpebral fissure area of the cornea. The cornea was insensitive to touch. The area of epithelial opacity stained with fluorescein. The anterior chamber was slightly shallow. The iris was gray-green, with normal markings. The pupil was 6.5 mm. in diameter and round and did not react to light or in convergence. The lens showed only a senile reflex with peripheral spokelike opacities.

External examination of the left eye gave essentially negative results. The pupil was 4.5 mm. in diameter and round and reacted normally to light and in convergence. The lens showed a senile reflex with cortical spokelike opacities.

Examination of the right fundus showed the optic disk to be of normal color, with a slight edema of the margins. The veins were all engorged and tortuous and showed variation in the size of the lumens in different areas. The arteries showed increased width of their reflexes. The veins were markedly compressed at the arteriovenous crossing. There was one flame-shaped hemorrhage lying just nasal to the disk. The macula appeared normal.

Examination of the left fundus showed the optic disk to be normal in color and outline. The vessels showed no engorgement or tortuosity, as shown in the right eye. Arteriovenous nicking was present, though not as marked as on the right. There were no hemorrhages or exudates. The macula was normal in appearance.

Slit lamp examination of the right eye indicated the superficiality of the keratitis e lagophthalmo. The cornea was otherwise normal. The anterior chamber was optically empty. The iris markings were normal. No pigment or cellular

depositions were present on the anterior capsule. The lens showed only healed peripheral spokes and nuclear sclerosis. The anterior portion of the vitreous was normal in appearance. The only abnormal findings in the left eye were the anterior and posterior cortical lamellar separation and waterslit formation in the lens.

The peripheral visual fields were normal. The right blindspot showed slight enlargement concentrically. The left blindspot was normal in size.

General physical and neurologic examination revealed an obese, senile woman with normal mental activity. On auscultation, directly over the forehead a loud swishing murmur was audible, most marked on the right side. This disappeared on digital compression of the right common carotid artery. The right cornea was anesthetic. The extraorbital cranial nerves showed no abnormalities of function. The heart and lungs were normal. Blood pressure was 170 mm. of mercury systolic and 90 mm. diastolic. The abdomen and extremities were normal, except for adiposity. Superficial and deep tendon reflexes were normal.
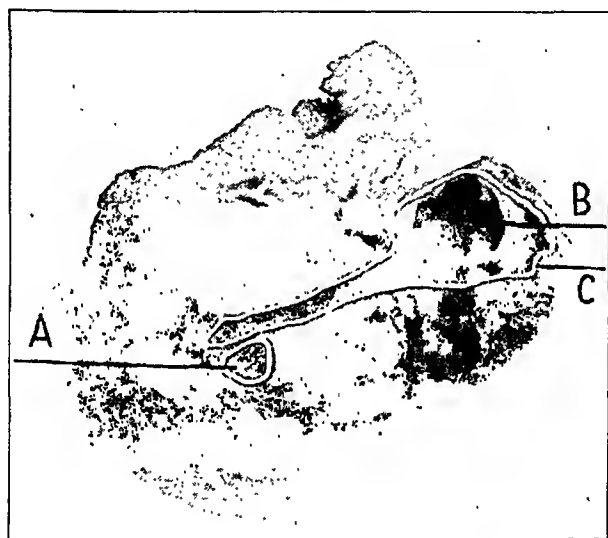
Fig. 1 (case 1).—Photograph of the inferior surface of the right cavernous sinus to show the arteriovenous fistula. *A* indicates the posterior entrance of the internal carotid artery into the cavernous sinus; *B*, the fistula in the internal carotid artery, and *C*, the edge of the wall of the cavernous sinus, part of which has been removed to show the fistula.

The Wassermann reaction was negative. There were 4,500,000 erythrocytes per cubic millimeter, a hemoglobin content of 87 per cent (Sahli), and 8,600 leukocytes per cubic millimeter, of which 70 per cent were polymorphonuclear cells, 28 per cent were lymphocytes and 2 per cent monocytes.

Urinalysis gave negative results.

Roentgenograms of the skull and orbits were entirely negative.

A diagnosis of spontaneous arteriovenous aneurysm between the right internal carotid artery and the cavernous sinus was made from the characteristic clinical findings.

On November 23, after the periorbital skin and lids were washed with soft soap and the conjunctiva on the right side with a solution of mercury bichloride,

the right lower lid was anesthetized with 1 cc. of a 2 per cent solution of procaine hydrochloride injected into the area of the lower orbital margin. The chemotic lower conjunctiva was incised horizontally at the junctions of the middle and nasal and middle and temporal thirds. The edema fluid was expressed digitally to allow replacement of the lower lid. This was accomplished, and the lower lid was held against the globe with black silk sutures, anchored to the forehead above the brow with adhesive tape. Ointment containing mercury bichloride and a patch were applied. The bandage was changed daily.

On November 25 a small conjunctival hemorrhage appeared on the lower nasal bulbar conjunctiva of the left eye, associated with increasing chemosis of the left lower palpebral and bulbar conjunctivas. On November 29 the exophthalmometer
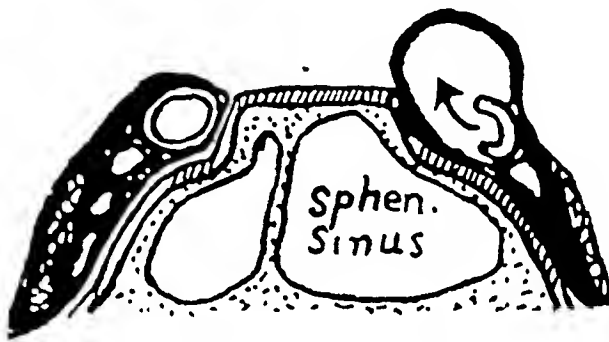
Fig. 2 (case 1).—Diagrammatic section through the anterior portion of the sella turcica in the region of the fistula.
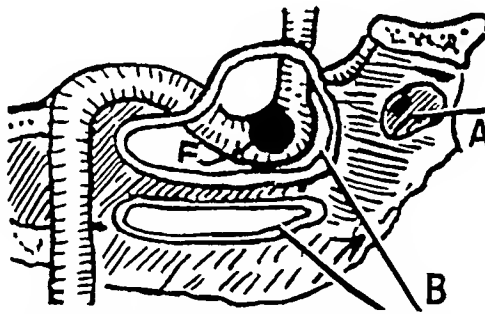
Fig. 3 (case 1).—Diagram showing the relations of the fistula. *A* shows the sphenoid sinus; *B*, the cavernous sinus, and *F*, the fistula.

readings were 25 mm. for the right eye and 23 mm. for the left eye (at 100 mm.), a decrease of the exophthalmos on the right and an increase on the left.

Examination of the fundi revealed no change in either eye from the previous findings. The vision in the right eye was the same; that in the left eye was 20/200 uncorrected and 20/100 corrected. The change was believed to be due to rearrangement of the venous circulation in the intercavernous sinuses.

On December 1 the patient became very drowsy and could not be aroused. Neurologically, no signs were present. The coma became deeper, and the patient died within a few hours.

Postmortem Examination (Dr. Otto Saphir).—The following observations were made relative to the brain and eyes: There was proptosis of both eyes. There

was edema of the lids and the conjunctiva. Below the margin of the right lower lid there were several well situated sutures. The upper and lower lids of both eyes showed bluish discoloration. Both conjunctivas showed, besides edema, a red discoloration and protrusion of two conjunctival folds on each eye.

The skull was extremely thick and hard. The dura was firmly adherent to the inner surface of the tabula interna. The superficial vessels of the cortical hemispheres were hyperemic. At the base of the brain an abnormality of the posterior cerebral artery was noted. This artery was seen to originate from the basilar artery as a delicate and small branch, forming the posterior communicans artery. From the region of the infundibulum much blood-tinged fluid exuded. A horizontal section through the region of the basal nuclei superior to the interventricular foramen showed no changes in the nuclei themselves. The lateral ventricles were partially filled with bloody fluid. The choroid plexuses on both sides were dilated and contained many small cysts in which there was a yellowish fluid. After removal of the corpus callosum there was found a blood clot in the third ventricle, filling the whole lumen. The cerebellum revealed on section a large dark area in which the normal substance was destroyed. This area was present in all lobes of the cerebellum and was seen to be connected with the fourth ventricle and the aqueduct of Sylvius, both of which were filled with clotted blood. The arteries of the base of the brain were filled with blood clots which continued in the more peripheral branches of the cerebral and cerebellar vessels. In addition, their intima contained many yellowish areas scattered throughout. The right cavernous sinus was markedly dilated. There was a communication between the internal carotid artery and the dilated sinus. At one point the latter was ruptured. The left cavernous sinus showed no changes. The region of the hypophysis on both sides and the region of the cavernous sinus were infiltrated with blood. There was clotted blood about the sella turcica.

The anatomic diagnosis according to Dr. Saphir's report was: marked arteriosclerosis of the basal arteries of the brain; encephalomalacia with hemorrhages involving the cerebellum; arteriovenous aneurysm of the right carotid artery and the cavernous sinus; arteriosclerosis of the aorta and coronary arteries; old endocarditis of the mitral valve; hypertrophy and dilatation of the heart (left ventricle); fatty infiltration of the myocardium (right ventricle); hyperemia of the liver; fatty infiltration of the pancreas; chronic cholecystitis with cholelithiasis and myofibromas of the uterus.

CASE 2.—V. S., a 48 year old white woman, entered the Illinois Eye and Ear Infirmary Aug. 22, 1938, service of Dr. S. J. Meyer. Two years previously she had injured the back of her head by a fall down a flight of stairs. She was unconscious for fourteen days after the accident. When she recovered consciousness she noticed a peculiar whirring noise in her head and prominence of the blood vessels of the right eye. The noise and prominent vessels persisted to the time of her admission to the clinic. With any exertion or on stooping, the noise became louder and the patient experienced vertigo. Roentgenograms of the skull taken at the Cook County Hospital after the accident were negative for fracture.

Vision, uncorrected, was 20/70 in each eye. Manifest refraction gave vision of 20/20 in each eye with a + 1.00 D. sph. + 0.50 D. cyl., axis 5 before the right eye and a + 1.50 D. sph. ⊃ + 0.25 D. cyl., axis 165 before the left eye. Jaeger's test type 1 was read at 15 inches (38 cm.) with each eye with a + 1.00 D. sph. addition.

The periorbita were normal in appearance. Each palpebral fissure measured 10 mm. in width. Exophthalmometer readings were 23 mm. for the right eye and 18 mm. for the left eye (at 104 mm.). The lids were normal.

The right bulbar conjunctiva contained medusa-head-like, dilated, tortuous veins. There was no chemosis. The palpebral conjunctiva, sclera and cornea were normal. The corneal sensitivity was intact. The anterior chamber was normal in depth and by slit lamp examination was seen to be optically empty. The iris markings were normal. The right pupil was 3 mm. in diameter and reacted normally to light and in accommodation-convergence. The lens and anterior part of the vitreous were clear. Ophthalmoscopic examinations of the right eye showed a type IV disk (Elschnig) with a temporal crescent. The margins and color of the disk were normal. The retinal veins were dilated to about twice their normal size. The macula was normal in appearance.

The anterior segment of the left eye was entirely normal by gross and by slit lamp examination. The pupil was 3 mm. in diameter and reacted normally to light and in accommodation-convergence. Ophthalmoscopic examination showed a type IV disk with a temporal crescent and normal retinal vessels and macula.
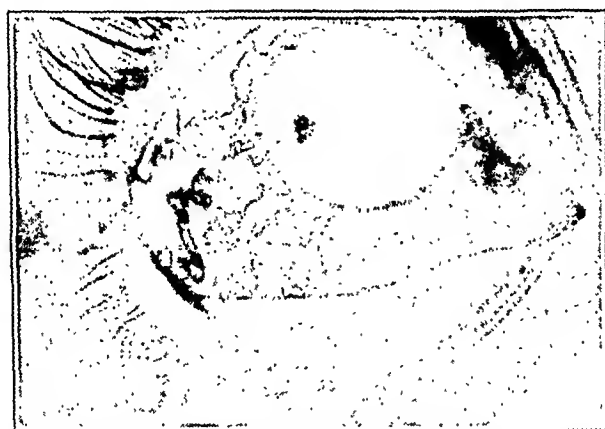
Fig. 4 (case 2).—Appearance of the right eye at the time of the first examination.

The accommodation near point was 36 mm. for each eye and for both together.

The convergence near point was 30 mm.; the proximal convergence base was 55 mm. With the Maddox rod the patient was orthophoric for distance but had 14 prism diopters of esophoria for near vision. The screen test showed no pareses or overaction of any muscles. A homonymous diplopia was present for near vision with the red glass test. At all subsequent examinations this convergence excess could not be elicited.

Visual fields, both peripheral and central, were entirely normal.

General physical and neurologic examination revealed only a bruit over the skull, most marked in the right frontal region. The blood pressure was 120 systolic and 80 diastolic. Roentgen examinations of the skull and orbits showed clouding of the right antrum with a polyp on the floor of the antrum.

Refraction with homatropine hydrobromide was done on September 2. The intraocular pressure, as measured with the Schiötz tonometer, was 28 mm. of mercury in the right eye and 26 mm. in the left eye. Retinoscopic and subjective examination gave vision of 20/20 in each eye with a + 1.25 D. sph. ⊃ + 0.50 D.

cyl., axis 5 before the right eye and a + 1.75 D. sph. ⊃ + 0.25 D. cyl., axis 165 before the left eye. Tonometric tension one hour after refraction was 20 mm. in the right eye and 23 mm. in the left eye. Postcycloplegic examination four days later gave the same vision with 0.25 D. sph. less in each eye. With reading additions of 1 D. sph. for each eye the patient could read Jaeger's test type 1 at 15 inches.

Laboratory findings were as follows: The Wassermann reaction of the blood was negative. The urine was normal. The hemoglobin content of the blood was 97 per cent, and there were 4,000,000 erythrocytes and 8,200 leukocytes, of which 70 per cent were polymorphonuclear cells, 28 per cent lymphocytes and 2 per cent monocytes.

Two unsuccessful attempts were made in September 1938 by Drs. C. A. Neymann and R. W. McNealy to visualize the vascular lesion roentgenographically. Twenty-five cubic centimeters of thorium dioxide was injected intra-arterially at each attempt.

On October 26 the intraocular tension was 35 mm. of mercury in the right eye and 22 mm. in the left eye. One drop of a 2 per cent solution of pilocarpine
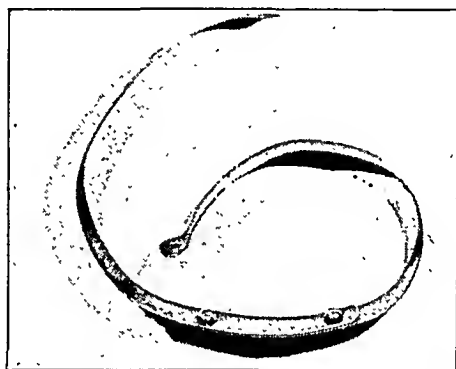
Fig. 5.—Cervical collar used in cases 2 and 4 (without padding).

was ordered four times daily in the right eye. On December 14 the tension was 35 mm. in the right eye and 32 mm. in the left eye. The use of pilocarpine five times daily in both eyes was then advised. On December 21 the tension· was 31 mm. in the right eye and 29 mm. in the left eye.

A cervical truss was then made and used for compression of the right common carotid artery. This was used four times daily, beginning with ten minute periods and increasing to about a half hour. No symptoms were produced by the compression. The bruit usually disappeared with compression, although occasionally it could be heard in the left ear. The compression was continued until ligation was performed on March 9, 1939, by Dr. C. H. Christoph. After careful dissection down to the common carotid artery, the artery was tied with heavy braided silk. Part of the omohyoid muscle was tied under the sutures to prevent cutting into the arterial wall. After the ligation, the bruit ceased. Recovery was uneventful, except for paralysis of the right vocal cord, which was due to surgical involvement of the right vagus nerve. Examination of the patient on March 25 revealed corrected vision of 20/20 in each eye. Tonometric tension was 19 in each eye. The exophthalmometer readings were 21 mm. for the right eye and 18 for the left eye (at 104 mm.). There was no change in the appearance of the conjunctival

or retinal veins. No bruit could be heard. The patient stated that when she exerted herself she sometimes heard a noise in the left ear. On June 21 she noticed the appearance of a mass beneath the area of the incision in the neck. She was seen a week later when a diagnosis of aneurysm of the common carotid artery was made, and she was referred back to the otolaryngologic service. On July 1, after local anesthetization, the neck was reopened by Dr. Lindon Seed, and a sac the size of a golfball was exposed. It was adherent to the surrounding tissues. It was tied off above and below with braided silk. The sac was opened, and an opening was found in the posterior medial wall of the common carotid artery. This was closed and the aneurysmal sac removed. In the opinion of Dr. Seed the aneurysm was saccular and had resulted from perforation of the wall of the carotid artery, probably by the previously placed suture. There was no connection with the internal jugular vein. The inferior thyroid, lingual and external carotid arteries were ligated with catgut. The internal jugular vein was ligated and cut at its lower end.

After the operation Horner's syndrome developed on the right side owing to paralysis of the sympathetic nerve on that side. On July 25 the right palpebral

Fig. 6.—Padded cervical truss used in cases 2 and 4.

fissure was 3 mm. less in width than the left. The right pupil was 2.5 mm. in diameter and the left 4 mm. Both reacted briskly to light. The exophthalmometer readings were 21 mm. for the right eye and 18 mm. for the left eye (at 104 mm.). The tonometric tension was 21 mm. of mercury in each eye. Visual fields and fundi showed no change from the original findings.

In retrospect, it is seen that in spite of the reestablishment of circulation after the first ligation there was relief from the bruit and normalization of intraocular tension. This speaks for the adequacy of partial ligation.

The complication of the formation of an aneurysmal sac as a result of perforation of the arterial wall is extremely unusual and is one of the rarest of complications. Two other complications also occurred in this case which may occur with this type of operation, namely, paralysis of the laryngeal nerve and Horner's syndrome.

CASE 3.—F. T., a 59 year old white man, was first seen at the Illinois Eye and Ear Infirmary on July 21, 1937, service of Dr. S. J. Meyer. On June 10, 1936, he was struck on the left parietal region with a blackjack during a robbery.

There was no unconsciousness. The left eye protruded, and the patient had severe headache on that side and a pounding noise in the ears, synchronous with the radial pulse. On June 30 a subconjunctival hemorrhage and marked chemosis occurred in the left eye. He was hospitalized at the Alexian Brothers Hospital in July 1936, and the left conjunctiva was incised to remove some of the chemotic fluid. Four weeks later the right eye became prominent and the right conjunctiva chemotic. In August 1936 the patient experienced diplopia, which persisted. A portion of the right chemotic conjunctiva was excised in October 1936. At the time of admission to the clinic the patient desired treatment for his right lower lid.

Vision was 20/200 in the right eye uncorrected and 20/100 in the left eye uncorrected. Manifest refraction gave vision of 20/20 in each eye with a + 1.25 D. sph. before the right eye and a + 1.75 D. sph. before the left eye; with a 2.50 D. sph. added the patient could read Jaeger's test type 1 at 14 inches (35 cm.). Tension was 23 mm. in each eye with the Gradle-Schiötz tonometer.

There was marked ectropion of the right lower lid with an exposed, red, rough conjunctiva. A symblepharon was present in the lower fornix. Exophthalmometer readings (Hertel) were 23.5 mm. for the right eye and 21 mm. for the left eye.

Fig. 7 (case 3).—Appearance of the right eye in July 1937.

A right esotropia of 10 degrees and right hypertropia of 8 degrees were present Excursions of the extraocular muscles in the six cardinal directions of gaze indicated pareses of the right external rectus, the right inferior rectus, the left superior rectus and the left inferior oblique muscles.

The right bulbar conjunctiva contained many large dilated veins. The cornea showed a faint superficial disturbance by slit lamp examination. A few precipitates were present on the posterior corneal surface. The anterior chamber was optically empty. The iris was normal. The pupil was 3 mm. in diameter and reacted normally in accommodation-convergence. The lens and anterior part of the vitreous were clear. Ophthalmoscopically the right disk was type II (Elschnig)) with a temporal scleral crescent. The veins were prominent and the macula normal.

The left bulbar conjunctiva showed engorged veins as on the right. The cornea, anterior chamber, iris and lens were normal. The pupil was 3 mm. in diameter and reacted normally. Examination of the fundi revealed slight elevation of the left disk, which was type II, with a temporal scleral crescent. There were eight or ten small hemorrhages along the peripheral course of the superior and inferior temporal veins. The macula was normal.

Examination of the visual fields gave entirely negative results.

Physical examination revealed a loud bruit, synchronous with the pulse, over the orbits and temporal regions. The blood pressure was 140 systolic and 84 diastolic. The Wassermann reaction of the blood was negative, and the urine was normal.

On August 9 a Kuhnt-Szymanowski operation was performed on the right lower lid by Dr. Jack Cowen. The cosmetic result was excellent.

A diagnosis of bilateral pulsating exophthalmos due to arteriovenous aneurysm in the cavernous sinus was made. On compression of the common carotid artery on the left the bruit disappeared, but the patient was unable to talk and experienced a tingling sensation in the opposite arm and hand. For this reason operation was believed contraindicated.

On September 30 refraction with eucatropine hydrochloride gave vision of 20/20 in each eye, with a + 2.00 D. sph. before the right eye and + 2.25 D. sph. before the left eye. Tonometric tension did not increase as a result of the pupillary dilatation with this cycloplegic. On postcycloplegic examination a + 1.75 D. sph. for the right eye and + 2.00 D. sph. for the left eye were ordered, with + 2.50 D. sph. additions.

On Nov. 21, 1938, the vision was 20/20 in each eye. During the past nine months the bruit had decreased markedly and no longer annoyed the patient. The diplopia persisted. The right pupil was 0.5 mm. larger than the left. The conjunctival vessels were much less prominent. The exophthalmometer readings were 22 mm. for the right eye and 21 mm. for the left eye. The bruit was still audible and disappeared on compression of the carotid artery.

On March 4 vision was 20/20 in each eye. Measurements of the field of diplopia and extraocular muscle were the same as on previous examinations.

On March 26 the screen test was done, and the following measurements at 1 meter were obtained.[1]

	6 X' 6 RH'		30 S' 10 RH'	
Patient's left	6 X' OH	20 S' 15 RH'	30 S' 20 RH'	Patient's right
	6 X' OH	18 S' 7 RH'	30 S' 30 RH'	

Fixation with right eye

With 20 prism diopters, base out, and 15 prism diopters, base up, in front of the left eye the patient felt comfortable and no longer experienced diplopia. A 26 prism diopter prism at axis 21 was then ordered as a slipover lens for the left eye. This was made up by J. C. Copeland of the Riggs Optical Company in the form of a plano meniscus prism with 6.00 D. base curves and cemented to the slipover lens. The patient had single binocular vision with good depth perception with the lens and experienced no chromatic aberrative sensations after the first day of its use.

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1. X indicates exophoria; RH., right hyperphoria, and S, esophoria. If a prime mark is used the test has been made at the near point.

This case is an example of spontaneous improvement in a case of bilateral pulsating exophthalmos in which operation had been previously considered but not done because of the results of digital compression. The visual result with prisms was excellent.

Fig. 8 (case 3).—Appearance of the patient in March 1939.
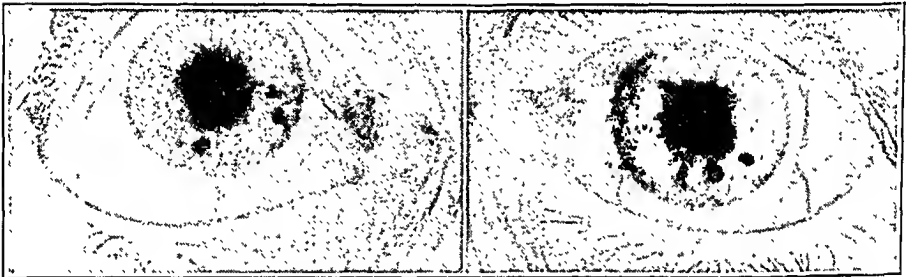
Fig. 9 (case 3).—Right and left eyes of the patient, showing marked improvement since 1937.
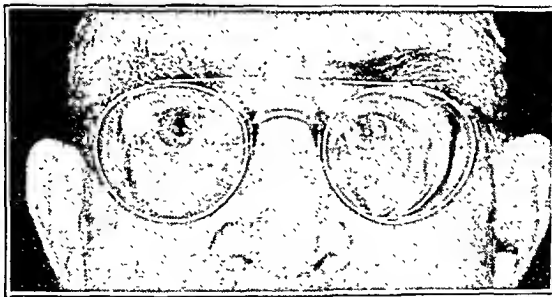
Fig. 10 (case 3).—Prism slipover in use.

CASE 4.[2]—W. McK., a 49 year old white woman, was seen by Dr. Harry S. Gradle on Feb. 24, 1939. Two months previously she had noticed a buzzing noise in her left ear, which persisted. Three weeks previously the left eyelids and

2. Drs. H. S. Gradle, E. Oldberg and G. H. Laing gave us permission to use this case report.

conjunctivas had become swollen. In the summer of 1938 she had bumped the left side of her head against the instrument board of an automobile when it stopped suddenly. On examination at that time by Dr. Grant H. Laing it was found that the left pupil was dilated, whereas at a previous physical examination on Oct. 14, 1937, the right pupil had been slightly larger than the left, but both had reacted normally to light.

Vision with a + 2.00 D. sph. correction for each eye was 20/20, and the patient could read Jaeger's test type 1. Tonometric tension (Schiötz) was 20 mm. of mercury in each eye.

The right eye was entirely normal by gross, biomicroscopic and ophthalmoscopic examinations. The pupil was 4 mm. in diameter and round and reacted normally to light and in accommodation-convergence.

Exophthalmometer readings (Hertel) were 13 mm. for the right eye and 16 mm. for the left eye (at 100 mm.). A loud bruit was heard over the orbits, particularly on the left side, and also in the left temporal region. Digital com-
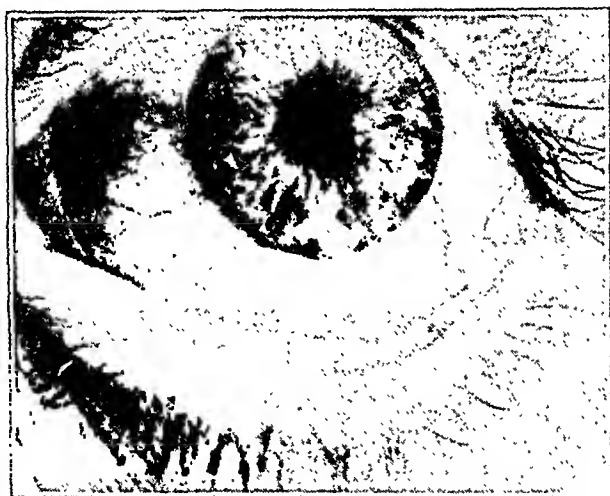
Fig. 11 (case 4).—Photograph of the left eye in March 1939.

pression of the left common carotid artery caused cessation of the bruit and the subjective noise. The left upper lid was edematous, particularly near the inner canthus. The outer half of the bulbar conjunctiva was edematous. The sclera was mildly injected. There was slight limitation of motion of the eye outward and possibly downward. The cornea and anterior segment were entirely normal. The pupil was 4 mm. in diameter and round and reacted normally to light and in accommodation-convergence. The inferior border of the left disk was somewhat hazy. The veins were slightly engorged and somewhat tortuous. The arteries were a little fuller than normal but not tortuous. The remainder of the fundus was normal.

Examinations of the peripheral and central visual fields gave entirely normal results.

A diagnosis of carotid-cavernous aneurysm was made, and the patient was given the cervical collar previously described (case 2) for prolonged compression of the common carotid artery.

The left exophthalmos and congestive signs slowly increased until the reading with the Hertel exophthalmometer was 25 mm. On November 19 the left internal

carotid artery was ligated just above the bifurcation of the common carotid artery by Dr. S. W. McArthur.

The patient made an uneventful convalescence except for some hemorrhage in the vitreous, which was clearing on examination on December 8. The bruit had completely disappeared. The exophthalmos had decreased 2 mm. The vision in the left eye was 0.25.

Group 1: True Pulsating Exophthalmos Due to Orbital Arteriovenous Aneurysm.—CASE 5.—J. C., aged 9 years, entered the hospital on Oct. 29, 1938, service of Dr. S. J. Meyer. Three weeks previously he had been struck between the right globe and lateral orbital margin by a prong of a pitchfork which was thrown from a haystack. The eye swelled shut immediately after the injury. The blood which had suffused under the skin of the upper lid had largely disappeared by the time the patient was admitted to the hospital.

Refraction without correction showed vision of 20/50 in the right eye and 20/25 in the left eye. Manifest refraction of the right eye gave vision of 20/20 and ability
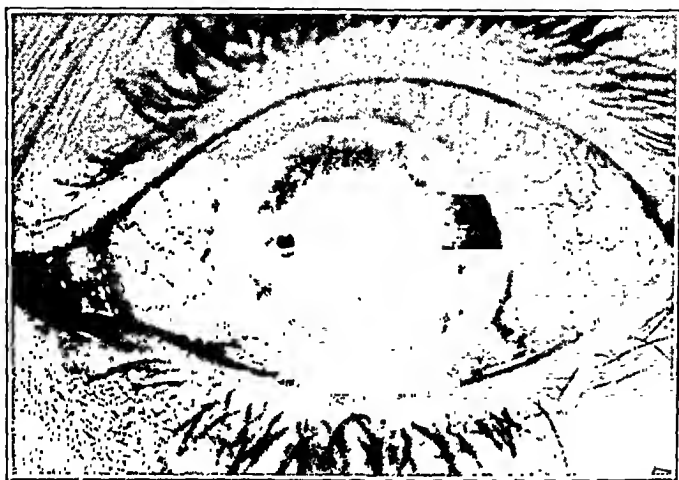
Fig. 12.—Photograph of the left eye taken on Dec. 7, 1939, shortly after ligation of the internal carotid artery. The appearance was similar to that observed shortly before operation.

to read Jaeger's test type 1 with a —0.50 D. sph. + 0.25 D. cyl., axis 140. Vision in the left eye with a + 0.25 D. cyl., axis 45 was 20/20, and the patient could read Jaeger's test type 1. Tonometric tension with the Schiötz tonometer was 26 mm. of mercury for the right eye, and 18 mm. for the left.

The right upper lid showed slight bluish discoloration, some swelling and dilated subcutaneous veins. Exophthalmometer readings were 22 mm. for the right eye and 15 mm. for the left. The right palpebral fissure was 8 mm. wide, while the left was 10 mm. There was no tenderness on pressure over the right orbital margin. A thrill was palpable, and a systolic bruit was audible over the area of the upper lid on the right. Digital compression of the right common carotid artery in the neck stopped the bruit and thrill.

The right palpebral conjunctiva was normal. The bulbar conjunctiva, however, contained markedly dilated and tortuous veins. The anterior segment was other-

wise entirely normal by gross and slit lamp examination. The corneal reflex was intact. Ophthalmoscopically the margins of the disk were slightly blurred. The arteries were normal in size. The veins were tortuous and dilated to about twice their normal size. The macula was normal in appearance. The left eye was entirely normal.

No diplopia could be elicited by the red glass test. Depth perception was normal, as tested with Guibor cards and the stereoscope.

Studies of the peripheral and central visual fields gave entirely negative results.

Roentgen examination of the right orbit to rule out possible fracture of the posterior wall or penetration by the pitchfork gave negative results.

Neurologic examination by Dr. B. Boshes showed no evidence of any involvement of nerves which might point to involvement of the cavernous sinus. The patient had two attacks of pyknolepsy during the examination. These had been present for the past six months. Complete physical examination otherwise gave negative results.

Refraction with atropine cycloplegia on October 17 gave 20/20 vision in each eye with a + 1.00 D. sph. ⊃ + 0.25 D. cyl., axis 105 before the right eye and a + 1.00 D. sph. ⊃ + 0.25 D. cyl., axis 90 before the left eye. Tension after refraction was 23 mm. in the right eye and 20 mm. in the left.

The urine was normal. Examination of the blood showed 4,900,000 erythrocytes per cubic millimeter, a hemoglobin content of 91 per cent and 9,600 leukocytes per cubic millimeter, of which 60 per cent were polymorphonuclear cells, 36 per cent lymphocytes and 4 per cent monocytes.

The exophthalmometer readings at the time of the patient's discharge, November 29, were the same as on admission.

A diagnosis of traumatic arteriovenous aneurysm of the right orbit was made. In view of the recency of the trauma, it was decided to wait for some time longer to get more vascular equilibrium in the orbit before attempting a surgical ligation of the venous part of the fistula in the orbit. Several attempts to get the child to return for operation, however, were unsuccessful.

The patient was seen by Dr. M. Hirschfelder, of Harrisburg, Ill., in October 1939, at which time the vision was 20/200 in the right eye and 20/20 in the left eye. Marked esotropia was present, with slight proptosis, pulsation and venous engorgement. The parents could not be persuaded to send the child back to Chicago.

Group 2: Pseudo Pulsating Exophthalmos Due to Orbital Angioma.—CASE 6.—S. K., a 34 year old white woman, presented herself at the Illinois Eye and Ear Infirmary, service of Dr. P. O'Connor, on Jan. 31, 1939. Ten years previously she had received a series of irradiations for hemangioma of the left orbit. For the past nine years she had been unable to see with the left eye and one year ago had noticed a white spot in her left pupil.

Vision in the right eye was 20/20 uncorrected, and the patient could read Jaeger's test type 1. Vision in the left eye was limited to perception of hand movements at 1 foot. Tension with the Schiötz tonometer was 22 mm. of mercury in the right eye and 23 mm. in the left eye.

The left lids and periorbital skin showed evidence of irradiation and thrombosis of the vessels of the skin. Exophthalmometer readings (Hertel) were 18 mm. for the right eye and 22.5 mm. for the left eye (at 100 mm.). The right palpebral

fissure was 10 mm. wide and the left 11 mm. when the patient looked upward. The left eye was visibly and tactually pulsating synchronously with the pulse. No bruit was heard.

The right eye was entirely normal on external and slit lamp examinations. The right pupil was 3.5 mm. in diameter and round and reacted normally to light and in accommodation-convergence. The right disk was normal and of type IV (Elschnig). The vessels and macula were normal in appearance.

External examination of the left eye revealed only a dense cataract. Slit lamp examination showed this to be due to anterior and posterior dense subcapsular opacities as well as nuclear changes. The left pupil was 3.5 mm. in diameter and round and reacted normally to light and in accommodation-convergence. General physical examination gave entirely negative results. The blood pressure was 121 systolic and 68 diastolic.

The left lens was extracted by the extracapsular method on February 1. Recovery was uneventful. On February 12 the left fundus was examined and found to be entirely normal.
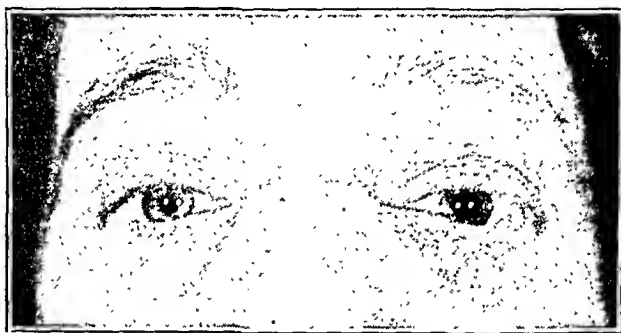
Fig. 13 (case 6).—Appearance of the patient after extraction of cataract.

TREATMENT AND RESULTS IN CASES OF CAROTID-CAVERNOUS
ANEURYSM

Beneficial results of treatment, whether surgical or nonsurgical, depend on two factors: (1) the prevention of short-circuiting of blood into the venous system and (2) a decrease of intracranial pressure for a sufficient length of time to promote thrombosis. Dandy has emphasized the second factor. Short-circuiting is prevented by slowing or obstructing the blood in the proximal arterial segment by compression or ligation, by slowing or obstructing the blood in the venous tributaries by ligation of the superior ophthalmic vein and by promotion of clotting by rest, injections of gelatin or the use of a cervical truss. Slowing or obstruction of the blood in the proximal arterial segment also favors the second factor.

Rest as a means of promoting clot formation is particularly important early, especially in the cases in which the exophthalmos is of traumatic origin. Of 27 cases in Locke's series, in which the results of rest were stated, 4 patients were cured, 10 were improved, 12 were not improved and 1 died. A number of other spontaneous cures have been recorded.

Sattler found 16 spontaneous cures in 322 cases, a percentage of 5.6. In our collected series there were 4 spontaneous cures, a percentage of 2.4. Seven other patients improved spontaneously, and 3 died without treatment.

Drugs administered to stimulate coagulation of the blood have been used by many authors. Those most used have been calcium salts and a solution of gelatin. The latter, advocated in warm 2 per cent solution by Lancereaux and Paulesco, is injected subcutaneously in doses of 100 to 250 cc. every four to eight days for a total of ten to twenty-five injections. In Locke's series of 16 cases in which this treatment was used, cure resulted in 5, improvement in 5 and failure in 6. In our group, 3 patients were treated in this manner. One improved, and 2 did not.

It is probably wise to continue conservative treatment until vascular compensation has occurred. Of course, when there is severe trauma with bleeding from the nasal orifices, ligation may have to be done immediately. If the patient in the average case is not treated, the vision may be lost, or thrombosis of the cavernous sinus with extension of the thrombus to the other venous sinuses may occur.

The only disadvantage of obstruction of the proximal segment of the artery is that the blood supply of the brain is thereby decreased, at times sufficiently to cause hemiplegia or even death. For this reason, every ligation should be preceded by compression to determine the adequacy of the anastomotic cerebral blood supply. Locke suggested that the latter may be tested as follows: If prolonged periods of compression stop the bruit and do not cause signs of cerebral anemia, beneficial results may be expected. Locke advised against too lengthy a course of compression in young persons, since it would increase the anastomotic circulation so much that on subsequent ligation the bruit would not be cut off. If compression of the carotid artery stops the bruit but causes signs of cerebral anemia, the compression should be continued in daily increasing amounts. If it neither stops the bruit nor causes signs of anemia, compression may be continued but without confidence of success on ligation.

Compression may be digital or by means of a cervical truss. Digital compression is performed by pressing the common carotid artery against the tubercle of the sixth cervical vertebra for gradually increasing periods of time three to six or eight times daily, beginning with one minute and increasing to about forty-five minutes for each period. The truss may be a collar of several types. Locke used one of wood and an elastic band with a padded front. May used a metal collar and Keegan a padded malleable iron one with an adjustable screw pad in a hinged front. Hennig used a padded phonograph spring. Wheeler used a wooden collar with a compression screw devised by Dr. J. L. Garvey. Harkness used a padded spring made of two bicycle trouser clips. The latter type was used by us in 2 cases.

By use of a cervical truss alone, the patient in 1 of our collected cases was cured and 3 were improved.

Ligation of arteriovenous fistula in the cavernous sinus differs from that in the extremities in that the involved artery is so extremely important in the maintenance of the cerebral circulation and in that so many inaccessible venous anastomoses are present. For this reason the ordinary principles of treatment do not easily apply.

There are two avenues of approach to ligation, arterial and venous. The arterial approach may be extracranial or intracranial. The extracranial method consists of ligation of the internal and the common carotid arteries or the latter's branches, singly, simultaneously or consecutively, or of plugging the internal carotid artery with long strips of muscle (Brooks) or with paraffin inserted at the origin of the artery in the neck. The intracranial approach is that of Dandy, recommended after failure of extracranial ligation.

Ligation may be partial or total. For the partial type many mechanical means have been employed, including Neff's, Halsted's and Matas' clamps and fascia lata. Dorrance, in two splendid papers, objected to the use of clamps, since they may injure the vascular endothelium and contribute to the danger of embolism.

Local anesthesia is employed for most ligations. The carotid artery is located and compressed with a clamp for one hour to determine the adequacy of the cerebral circulation, during which time the wound is covered with moist gauze. If no ill effects are observed, one of the various aforementioned types of ligation is performed. During the compression or after ligation, the patient may experience faintness, nausea or vomiting, tinnitus, partial loss of vision, headache, contralateral hemiplegia, convulsions and sensory disturbances. Most of these improve and usually disappear. In some patients the sensory and motor changes are permanent. Blindness, aphasia and mental deterioration remain in some. In addition to the few who died during or shortly after the operative procedure, a number have suffered hemiplegia or death during the period from the fifth to the tenth days after operation. For this reason the patient should be at absolute rest in bed for ten days to two weeks after operation.

The choice of whether to ligate the common or the internal carotid artery is not yet settled. In Dorrance's series of 275 cases, ligation of the internal and common carotid arteries closely approximated each other, with slightly better results with the ligation of the common carotid artery. A few more recurrences occurred after ligation of the internal carotid artery.

The majority of 25 opinions from King's questionnaire advocated slow ligation of the common carotid artery, with fascia lata, a silver band, Neff's clamp or Parham's band.

TABLE 1.—*Results of Treatment in Cases Collected up to 1927, Including Dorrance's Series and Results of King's Questionnaire*

Treatment and Results	Locke 1809 to 1923	Harkness	Dorrance	King
No treatment:				
No. of cases	..	..	46	6
Cure	..	..	13	..
Improvement	..	..	..	3
Failure	..	..	5	1
Fatal results	..	..	3	2
Results not stated	..	..	25	..
Rest and medication:				
No. of cases	28	4	15	..
Cure	4	} 1	0	..
Improvement	10	}	13	..
Failure	12	2	2	..
Fatal results	1	..	..	..
Results not stated	1	1	..	..
Compression:				
No. of cases	106	1	13	..
Cure	} 28	} 1	5	..
Improvement	}	}	3	..
Failure	..	78	5	..
Fatal results	0	..	..	..
Injections of Gelatin:				
No. of cases	16	..	15	..
Cure	5	..	5	..
Improvement	5	..	1	..
Failure	6	..	9	..

Treatment and Results	Locke 1809 to 1923	Harkness	Dorrance Partial (2 steps)	King Total (1 step)
Ligation of common carotid artery:				
No. of cases	234	15	71 16	21
Cure	}	}	37 }	}
Improvement	}154	}14	12 } 16	}17
Failure	56	0	12	1
Fatal results	21	1	..	3
Results not stated	3	..	..	..
Recurrence	..	..	10	..
Combined ligation of common carotid artery and other vessels.				
No. of cases	..	..	9	..
Cure	..	..	5	..
Failure	..	..	3	..
Recurrence	..	..	1	..
Secondary ligation of common carotid artery:				
No. of cases	..	..	2	..
Cure	..	..	1	..
Failure	..	..	1	..
Ligation of internal carotid artery:				
No. of cases	38	6	44	11
Cure	8	} 5	25	}11
Improvement	25	}	8	}
Failure	2	1	2	..
Fatal results	3	1	..	..
Recurrence	..	..	9	..
Combined ligation of internal carotid artery and other vessels.				
No. of cases	..	1 (with external)	13	..
Cure	..	}	6	..
Improvement	..	} 1	3	..
Recurrence	..	..	4	..
Secondary ligation of internal carotid artery:				
No. of cases	..	..	12	..
Cure	..	..	5	..
Improvement	..	..	4	..
Failure	.	..	3	..
Bilateral ligation of carotid artery:				
No. of cases	21	..	..	..
Cure or improvement	13	..	..	..
Failure	4	.	..	..
Fatal results	3	..	..	..
Results not stated	1	..	..	..
Ligation of orbital vein:				
No. of cases	19	1	11	2
Cure	8	..	3 (2 orbital)	1
Improvement	5	1	2	..
Failure	5	..	6	2
Fatal results	1	..	..	..
Ligation of orbital vein combined with ligation of carotid artery:				
No. of cases	24	..	12	..
Cure	9	..	4	..
Improvement	8	..	4	..
Failure	3	..	1	..
Fatal results	4	..	3	..
Ligation of orbital vein after failure of ligation of carotid artery:				
No. of cases	..	1	15	3
Cure	..	..	5	..
Improvement	..	..	3	..
Failure	..	} 1	4	} 3
Fatal results	..	}	3	}

Treatment and Results	No. of Cases	Cure	Improvement	Failure	Fatal Results	Results Not Stated	Recurrence
No treatment, rest alone or medicine alone	28	4	7	11	3	3	..
Compression alone (cervical truss)......	4	1	3	..	..	..	..
Injections of gelatin alone..............	3	..	1	2	..	..	..
Ligation of common carotid artery alone:							
(a) Partial (2 stages)...................	5	4	..	..	..	..	1
(b) Total (1 stage).....................	29	13	9	6	1	..	6
Ligation of common carotid artery:							
(a) with ligation of internal carotid artery	5	2	3	..	..	..	..
(b) with ligation of superior thyroid artery	1	1	..	..	..	..	..
(c) with ligation of internal jugular vein	3	3	..	..	..	..	..
(d) with ligation of external carotid artery	1	1	..	..	..	..	..
Secondary ligation:							
(a) ligation of internal and common carotid arteries after failure of ligation of orbital vein..................	1	..	1	..	..	..	..
Ligation of internal carotid artery:							
(a) partial	2	2	..	..	..	..	..
(b) total	28	13	6	7	1	1	3
Ligation of internal carotid artery:							
(a) with ligation of jugular vein......	1	1	..	..	..	..	..
(b) with ligation of external carotid artery	3	1	1	..	1	..	..
Secondary ligation of internal carotid artery:							
(a) after ligation of common carotid..	4	2	1	1	..	..	..
Bilateral ligation of carotid artery......	4	3	..	..	1	..	..
Ligation of orbital vein..................	3	1	1	1	..	..	..
Ligations of orbital vein:							
(a) with ligation of common carotid artery	2	2	..	..	..	..	..
Secondary ligations of orbital vein:							
(a) after ligation of internal carotid artery	1	..	..	1	..	..	..
(b) after ligation of common carotid artery	4	4	..	..	..	..	..
(c) after ligation of internal and external arteries	1	1	..	..	..	..	..
(d) after ligation of internal and common arteries	1	1	..	..	..	..	..
Ligation of external and superior thyroid arteries secondary to recurrence after ligation of common carotid artery....	1	1	..	..	..	..	..
Intracranial ligation of internal carotid artery	2	1	1	..	..	..	..
Ligation of internal jugular vein after ligation of carotid artery..............	2	..	..	2	..	..	..
Ligation of common and internal carotid arteries secondary to ligation of orbital vein	1	..	1	..	..	..	..
Ligation of common and internal carotid arteries after Brooks' operation..	1	1	..	..	..	..	..
Brooks' operation	1	1	..	..	..	..	1
Brooks' operation secondary to recurrence after ligation of common carotid artery	1	1	..	..	..	..	..
Carotid artery not stated................	10	2	..	..	..	8	..
Treatment not stated or patient not yet treated	12	..	..	..	..	..	..

In our series, ligation of the common carotid artery alone was done in 34 cases. Cure resulted in 17 cases (50 per cent), improvement in 9, failure in 6, death in 1 and recurrence in 7.

Ligation of the internal carotid artery alone was done in 30 cases. Cure resulted in 15 cases (50 per cent), improvement in 6 (2 patients had hemiplegia), failure in 7, death in 1 and recurrence in 3. The result in 1 case was not stated.

These results indicate no advantage of one over the other.

It has been shown by Blackman, Dorrance, Matas and many others that after ligation of the common carotid artery there is a reversal of blood flow in the external carotid artery. Almost half of this recurrent flow, according to Dorrance, comes from the superior thyroid artery. Part of it comes from anastomoses between the descending branches of the occipital trunk and the deep cervical branches of the costovertebral trunk, and the lingual, facial, occipital and temporal arteries, with the corresponding arteries of the opposite side. Dorrance expressed the belief that this reverse flow is important in preventing both cerebral anemia and the reversal of flow in the distal segment of the artery, which would occur if the internal carotid artery were ligated. He therefore advocated first ligation of the common carotid artery, then, if necessary, of the superior thyroid and occipital arteries. Later the external trunk itself could be ligated if necessary.

In spite of the argument that ligation of the common carotid artery offers greater security, it would appear to the casual observer that the restoration of blood flow through the internal carotid artery by collateral circulation is just the effect one is trying to overcome. Actually, when the internal carotid artery itself is ligated, the reversed flow through the aneurysmal opening from the circle of Willis tends similarly to continue the syndrome of pulsating exophthalmos. Since there is a flow of blood through the aneurysmal communication in either case, there seems to be little mechanical advantage of ligation of the common carotid artery over that of the internal carotid artery, or vice versa. To us it appears that the added safety of ligation of the common carotid artery makes it the better choice.

Dorrance stated that the common carotid artery is the more logical choice for ligation because of the relations of the carotid sinus to the two types of ligation. If the internal carotid artery is ligated, there is dilatation of the carotid sinus and a subsequent fall in blood pressure. The latter adds to the danger of cerebral anemia still further. If the common carotid artery is ligated below its bifurcation, where the sinus is located, this danger is avoided.

Esteban pointed out that a possible disadvantage of ligation of the common carotid artery is the increased possibility of embolism due to the slow reversed flow through the external carotid artery into the internal carotid artery.

Bilateral ligation of the carotid arteries was reported by C. H. Sattler in 14 cases, with 3 deaths. Locke reported 21 cases, with 3 deaths. In our group there were 3 cures and 1 fatality in 4 cases in which bilateral ligation was done.

On the venous side the surgical approach consists of ligation or extirpation of the ophthalmic veins, use of diathermic coagulation of the veins (Fioletov), injection of sclerogenic solutions and direct ligation of the veins after enucleation. These act by causing thrombosis in the venous channel, extending to the region of the fistula.

Of 3 cases in our group in which orbital venous ligation alone was performed, cure resulted in 1, improvement in 1 and failure in 1.

Some authors, especially Continental ones, have ligated the internal jugular vein in conjunction with ligation of the carotid artery (Holman, Laméris, Verkerk and Guazzieri). Cure resulted in all of 4 reported cases.

For the orbital arteriovenous communications, the vessels may be approached transconjunctivally between the globe and the lateral orbital wall (Wheeler) or by the Krönlein operation or one of its modifications.

From the results observed by us in our series, we advocate first rest and compression, with observation of the vision and general condition, then partial or total ligation of the common carotid artery. Later, the superior thyroid or external carotid artery can be dealt with if necessary.

Spaeth, in his recent book on ophthalmic surgery, pointed out that roentgenologists have obtained satisfactory results with high voltage roentgen therapy in cases of carotid-cavernous aneurysm. This method has as yet had insufficient trial. Inability to limit the area of reaction to the desired small area and the possibility of extension of the thrombotic process as a result of irradiation seem to be reasonable points against its use.

SUMMARY

The literature on pulsating exophthalmos is brought up to date. One hundred and sixty-five cases have been added to the gathered literature, together with 6 of our cases.

Increased intraocular tension in some of these cases is emphasized, since most of the English literature completely disregards this important point.

Principles of treatment are discussed, since patients with this condition often present themselves to the oculist rather than to the general surgeon.

904 West Adams Street.

58 East Washington Street.

DISCUSSION

Dr. F. Bruce Fralick, Ann Arbor, Mich.: Drs. Meyer and Sugar have left little to be added to this subject in the light of the present knowledge concerning it. To the 6 cases of pulsating exophthalmos reported by them, I wish to add the summaries of 8 more, previously unreported cases of the same condition seen between the years 1924 to 1939 in the University Hospital, Ann Arbor.

(Eight cases were briefly summarized.)

That this condition is rarely seen is illustrated by the fact that these 8 cases represent a frequency of 1 case of pulsating exophthalmos to every 22,500 patients seen in the clinic.

The observation of Kattan that in the presence of carotid-cavernous aneurysm the vision may remain normal for over twenty-five years, even when accompanied by rather marked engorgement of the retinal vessels, illustrates well Whitnall's findings in regard to the venous drainage of the eyeball and orbit. He states that the central vein of the retina opens most frequently separately into the cavernous sinus, rarely into the superior or even the inferior ophthalmic vein, but that it always has at least one side connection, commonly with the superior ophthalmic vein. This anastomosis is not only important in carotid-cavernous aneurysms but explains why one does not have the clinical picture of occlusion of the central retinal vein in thrombosis of the cavernous sinus.

For the sake of completeness of the discussion of pulsating exophthalmos, a little more might be said in regard to pulsation of the eyeball associated with defects in the wall of the orbit, as pointed out by the late John Wheeler. He stated that these bony defects may be due to a congenital arrest of development or an accompaniment of plexiform neurofibromatosis of the orbit (Recklinghausen's disease) and that in this condition the bony defect may be congenital or the result of surgical removal of the orbital roof, as in the Naffziger operation for malignant exophthalmos. Wheeler also pointed out certain important differential diagnostic points between arteriovenous communications and orbito-cranial communications, which one should keep in mind when a patient with pulsating exophthalmos is presented. In orbitocranial communication, the pulsation is more evident to the examiner on direct observation, while in arteriovenous communication the pulsation is seldom seen but may be elicited by compression of the globe and orbital tissues. The pulsation is synchronous with the pulse in both conditions. The pulsation is not accompanied by the annoying bruit, as is always the case in arteriovenous communication. There is an absence of the markedly dilated veins of the eyeball, lids and surrounding tissues as seen in arteriovenous communications.

All the diagnostic aids possible must be used to differentiate the types and location of the lesions causing pulsating exophthalmos if one is to obtain the highest percentage of good results for such patients.

Dr. Edmund B. Spaeth, Philadelphia: In a presentation on any subject which is as exhaustive as is this, one could select for a set discussion any one of many different subdivisions or points of interest which are developed. Questions on the anatomic picture, the etiologic factors and the mechanics of the condition, the rationale of the therapy utilized and the gross local as well as the gross distant pathologic involvement all are of equal importance with the problem which I should

like to emphasize, namely, differential diagnosis. Even this is to be further limited in that only those cases are being considered for differentiation in which there are one or more of the following common factors: a history of trauma, a bruit or at least a pounding or throbbing sensation, exophthalmos, definite visible pulsation and modification of the signs and symptoms by temporary pressure on the centripetal blood vessels or by changes in the position of the patient's head. In the final analysis, when considering vascular conditions alone the greatest single diagnostic necessity is the differentiation of an orbital, i. e., arteriovenous, aneurysm from an intracranial aneurysm of one of the larger intracranial cerebral blood vessels. Möller, who studied 555 cases of the latter condition, stated that in none of these was choked disk found, bulbar protrusion was rare, oculomotor paralyses were quite common and true pulsation was never seen. The authors' subgroups, as they arranged them, are proper and clearcut.

(Six case histories were briefly presented.)

Dr. T. L. Terry, Boston: In 1934 Mysel and I reported a case of pulsating exophthalmos resulting from an abnormal arteriovenous communication in the neck between the internal jugular and the internal carotid artery. Since that report was made, there have been several developments. The pulsating exophthalmos has recurred, as Reed predicted in his discussion of the original report. This Reed based on the spontaneous onset attributable to congenital defects, and such congenital defects are usually multiple. The patient had resumed heavy labor as a hod carrier. The roentgen localization by means of injection of thorium dioxide proved faulty in that another patient with an arteriovenous communication in the cavernous sinus showed a similar shadow in the neck with the use of the same technic. In spite of Dandy's criticism, it seems most logical to believe that the abnormal communication, as originally reported, was located in the neck, because whirlpools and eddies of arterial blood were seen in the internal jugular vein, a condition I have seen only near the location of arteriovenous communications, since a mixture of arterial and venous blood would be complete a relatively short distance central to the aneurysm. It must be remembered that the murmur was loudest in the upper part of the neck and was slightly audible over the skull and the eye and that the amount of exophthalmos was never large. Although the pulsating exophthalmos has recurred, it is not as extensive as it was previous to the operation.

Localization of abnormal arteriovenous communications is important because the communication is not always intracranial. It may be intraorbital as shown by the case reported by an associate and myself in 1938. In event the communication is not in the cavernous sinus, it may be removed. On the basis of experience in several instances, it was found that the ultimate vision of the exophthalmic eye is often reduced. If that conclusion is correct, one should consider sacrificing the eye if by so doing the aneurysm can be eradicated. This is a surgical possibility if the aneurysm is in the orbit behind the globe. Verhoeff successfully obliterated the aneurysm causing a pulsating exophthalmos by enucleation and by ligation of the orbital vessels.

The abnormal arteriovenous communication can be visualized and thereby accurately located by use of radiopaque substances injected into the artery. The correct technic for getting this result appears to be that

used by Dr. J. C. White, a neurosurgeon of the Massachusetts General Hospital. Relatively recently he exposed the carotid artery in a patient with typical extensive pulsating exophthalmos and placed a band of fascia lata around the artery. The fascia lata was made to constrict the vessel by successively stitching it tighter. After the artery was occluded considerably and the flow of blood through it slowed down, 10 cc. of thorium dioxide was injected rapidly into the vessel distal to the fascia lata and the roentgen film exposed simultaneously with the injection.

Dr. Philip M. Lewis, Memphis: I wish to take just a few moments to add a brief discussion of 3 cases from the ophthalmic service of the John Gaston Hospital of the University of Tennessee.

In the first case that I will discuss the pulsating exophthalmos was due to trauma. Ligation of the superior ophthalmic vein was first tried. It caused no benefit; in fact, it resulted in great harm, because the cornea immediately sloughed. After that the internal carotid artery was ligated. The eye had to be removed. Six months later the bruit returned. The patient was then lost from observation. She was 61 years of age.

The second patient, aged 25, had two distinct injuries to the head. The first one occurred six weeks before the second one and resulted in a rupture of the globe, causing him to lose his eye. Ten days later he was attacked by robbers with a blackjack, and almost immediately afterward, as he expressed it, his eye popped out of his socket, so that he was unable to close his eyelids. He did not complain of any noise in his head. When he was seen his eye was greatly proptosed. He had an ulcer of the cornea of the lower portion, and his vision was reduced to 20/100. Ligation of the internal carotid artery was done as soon as it was found that compression of the artery caused no untoward symptoms, and the eye was saved. The patient regained good vision, and everything in his case has been all right.

The third patient, aged 41, is still under observation and has afforded a most interesting study. He gave a history of severe headache for two weeks before admission to the hospital. Six days previously he first noticed a noise in the left side of his head, and the following day his left eye was swollen; the swelling greatly increased, and a throbbing pain was present in his eye all the time. Pain was also present in the left side of his face and upper teeth. He stated that he had never had any injury and had had no previous ocular trouble. Physical examination gave negative results except for the ocular findings. The eye was greatly proptosed, so that the entire cornea and most of the bulbar conjunctiva were constantly exposed. Its entire surface was dry and opaque. A superficial ulcer covered the entire cornea. The conjunctiva was edematous and bleeding from several points. The lids were firm and tense. They pulsated with each beat of the pulse. A bruit could be heard over the left brow and temple. Compression of the left carotid artery stopped the bruit, the pulsation and also the throbbing pain. Stereoscopic roentgenograms of the skull were negative. The reaction to the Kahn and Kline tests of the blood were 4 plus. The spinal fluid was normal and also negative for syphilis.

The condition of the eye rapidly became worse, so that it was evident that it would have to be removed. Ligation of the internal carotid

artery was followed by an immediate improvement of all symptoms. A few days later the eye was eviscerated, at which time a purulent infection was found to be present throughout the entire eye. Following this operation the reaction was severe, and pus drained from the scleral cavity for several weeks.

About three weeks after ligation of the carotid artery the patient complained of increasing headaches. Lumbar puncture showed the spinal fluid to be cloudy and under an increased pressure of 150 mm. of water. The cell count was 915 per cubic millimeter. Seventy-three per cent were polymorphonuclear cells and 27 per cent lymphocytes. The culture was first reported positive for nonhemolytic streptococci. Subsequent cultures failed to show this organism but instead a gram-negative bacillus, which proved to be Bacillus alcaligines. The presence of the organism in both cultures was probably due to contamination. None of the usual signs of meningitis were present, and the patient was not extremely ill. Sulfanilamide was given in large doses, and after a course was given he was also given sulfapyradine for a while.

The spinal fluid gradually cleared, and the headache ceased. The patient then complained for the first time of poor vision in his right eye. Examination of the fundus showed partial primary atrophy of the optic nerve, the exact cause of which is somewhat doubtful. The entire temporal field of vision of this eye is lost, and his vision is 20/200. Probably pressure from the aneurysm on the central portion of the chiasm was responsible, but possibly it was caused by a localized meningitis involving the anterior horn of the chiasm on its medial side. The presence of an abscess of the brain is seriously suspected by the attending neurologists who have examined the patient. The spinal fluid count was 50 per cubic millimeter when taken recently. The patient says he feels fine, and apparently he is going to recover. He is still confined to the hospital, where he has now been for over ten weeks.

Syphilitic involvement of the wall of the internal carotid artery, with eventual rupture into the cavernous sinus, was the probably cause of the pulsating exophthalmos in this case. Bruit and the other symptoms have disappeared, but I think that it is an interesting case from the standpoint of the development of this meningeal condition.

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Correspondence

INTERSTITIAL KERATITIS AND RIBOFLAVIN DEFICIENCY

To the Editor:—A letter by Dr. L. V. Johnson and Mr. R. E. Eckardt was published in the March number of the ARCHIVES under the heading "Is the Onset of Interstitial Keratitis Related to Riboflavin Deficiency?" (page 631). This letter criticizes us for the wording of a news release published in the *Cleveland Press* of Feb. 3, 1940 and does not refer to our publication on the subject entitled "Ocular Manifestations of Ariboflavinosis" (*Pub. Health Rep.* 55: 157 [Jan. 26] 1940). We feel that we should call attention to the fact that the letter of Dr. Johnson and Mr. Eckardt does not refute any of the evidence in our paper. It should be unnecessary for us to point out that we have no control over the public press.

We do not desire to enter into a controversy on the subject, and we feel that our published observations are sufficiently clear, sound and conservative. Our only reason for writing this reply is that the following statement from the letter of Dr. Johnson and Mr. Eckardt may cause some ophthalmologists to neglect to use riboflavin in the treatment of keratitis.

Ophthalmologists will be disappointed with clinical results if, after reading the accounts widely distributed through the newspapers of all cities, they attempt to give relief to their patients by the use of preparations containing the riboflavin equivalent of a twentieth of a quart of milk!

This statement is misleading, because in our publication we stated that we were using pure synthetic riboflavin in daily doses of 5 to 15 mg. When used in such amounts we have seen strikingly beneficial results in more than 50 cases of keratitis. Improvement is so much faster and better than with any other method of treatment that we want to urge ophthalmologists to test thoroughly the value of sufficient amounts of riboflavin in the treatment of their patients with keratitis.

H. D. KRUSE, M.D.
Milbank Memorial Fund, New York.

V. P. SYDENSTRICKER, M.D.
University of Georgia Medical School, Augusta.

H. M. CLECKLEY, M.D.
University of Georgia Medical School, Augusta.

W. H. SEBRELL, M.D.
United States Public Health Service, Washington, D. C.

Notices

A NEW FEATURE OF THE ARCHIVES

Question and Answer Department.—To enable readers of the ARCHIVES to obtain information, if available, on a problem which has presented itself in their practice, a new department, called Questions and Answers, will be established, under the direction of Dr. W. L. Benedict.

This plan has been carried out with success in one of the European ophthalmic journals and should be of service to the readers of the ARCHIVES.

Questions are to be sent to Dr. W. L. Benedict, the Mayo Clinic, Rochester, Minn., accompanied by the sender's name or, if preferred, initials. The questions and the answers will be published in subsequent numbers of the ARCHIVES.

News and Notes

EDITED BY W. L. BENEDICT

SOCIETY NEWS

Meetings of Specialists.—The Tennessee Academy of Ophthalmology and Otolaryngology held its annual meeting in Chattanooga, April 9, in conjunction with the annual meeting of the Tennessee State Medical Association. Guest speakers were Drs. Harry S. Gradle, Chicago, on "Secondary Glaucoma," and Albert C. Furstenberg, Ann Arbor, Mich., on "Acute Infections of the Mouth, Pharynx, Cervical Region and Mediastinum." Dr. Wesley Wilkerson, Nashville, was elected president of the academy; Dr. J. V. Hodge, Kingsport, vice president, and Dr. William D. Stinson, Memphis, secretary.

Home Study Course.—The home study course in the fundamentals of ophthalmology and/or otolaryngology that will be conducted by the American Academy of Ophthalmology and Otolaryngology will start on Aug. 1, 1940. Registration must be made through the executive secretary, Dr. W. P. Wherry, 1500 Medical Arts Building, Omaha, not later than July 1.

UNIVERSITY NEWS

Course on Ocular Conditions Available to Lay Workers.—A course entitled "A Survey of Eye Conditions" will be given at the summer session of New York University for workers in the fields of education, social welfare and nursing and in allied fields. The course, which has been offered since 1932 in cooperation with the Bureau of Service for the Blind, New York State Department of Social Welfare, aims to give a knowledge of ocular conditions as related to problems of general health and welfare, with emphasis on the need for conservation of sight and prevention of blindness. Information about the lectures may be obtained from Miss Ruth McCoy, Bureau of Services for the Blind, New York State Department of Social Welfare, 205 East Forty-Second Street, New York.

Abstracts from Current Literature

Comparative Ophthalmology

IRITIS (WHITE EYE) IN FOWLS. J. E. R. McDONAGH, Brit. J. Ophth.
23: 659 (Oct.) 1939.

Iritis in fowls, or "white eye," is one of the manifestations of the
disease complex which is most commonly known as "fowl paralysis."
The other manifestations are paralysis, leukemia and lymphocytomas.
The condition results from the activity of the pathogenic developmental
or mutation forms of Bacillus coli communis, which have their habitat
in the intestinal canal.

The color of the iris changes to varying shades of gray, first in one
eye and then in the other. Synechiae form, the pupils become contracted
and finally obliterated and the animal is rendered blind.

The first histologic change in the iris consists of a perivascular invasion
of leukocytes, which is most marked in the anterior part of the iris,
where the striped sphincter pupillae muscle is found. As the severity
of the infection increases, the iris gradually becomes so densely infiltrated
that it is difficult to describe its structure. The pigment epithelium swells
and degenerates as the severity of the iritis increases. The pigment
particles agglutinate into balls, which wander into the iris tissue or into
the posterior chamber. The normal fat of the iris disappears. Similar,
but less marked, changes occur in the ciliary body and its processes. A
migration of cells and pigment into the vitreous may occur, with the
formation of a fine network of connective tissue. The anterior chamber
is filled with plasma, which contains a varying number of leukocytes.
Cells are found covering the fibers of the ligamentum pectinatum and
infiltrating the walls of Schlemm's canal, to the extent of producing
wartlike masses which project into the canal. The choroid is but little
affected. The vessels are dilated, and the cells of the pigment epithelium
swell and show signs of wandering. The retina is never attacked
primarily. The papilla and pecten may be infiltrated with leukocytes.
The iridocyclitis which occurs in fowls is not to be differentiated from
the manifestation of disease which appears in man as a symptom of
intestinal toxemia.

The article is illustrated.

W. ZENTMAYER.

Cornea and Sclera

AN UNUSUAL CONDITION OF THE POSTERIOR SURFACE OF THE CORNEA
(POSTERIOR HERPES OF THE CORNEA). L. STAX, Brit. J. Ophth.
23: 622 (Sept.) 1939.

A well built youth, aged 18, had acne vulgaris and comedos over
the face. He never had herpes labialis. With the biomicroscope, there

was seen in the upper half of the right cornea a longitudinal grayish white area, and in an irregular row in the center of this band were a few clear circular holes. The band was located in the position of the corneal endothelium, and the clear areas caused the beam of light to bulge into the anterior chamber. They looked like small vesicles, but the posterior surface could not be seen, and one was left with the impression that the clear areas were ruptured vesicles. A similar condition was present in the lower half of the left cornea.

About two months later, in the right eye, the opacity stretched from the center of the cornea to about "9 o'clock" on the edge of the semi-dilated pupil. The gray area was of uneven thickness, being denser at the temporal end, and the clear areas were punched out, with raised edges. It appeared as if the layer of endothelial cells had become curled forward and folded over.

In the left eye the condition was situated at "6 o'clock" on the edge of the iris. Four years later there was a suggestion of interstitial changes in the right cornea. Vision in the right eye was 6/9 and in the left 6/6.

The literature on allied conditions is reviewed.

The article is illustrated.

W. ZENTMAYER.

Glaucoma

ON THE TREATMENT WITH "GLAUCOSAN" OF CASES OF GLAUCOMA OPERATED UPON WITHOUT SUCCESS, AND OF COMPLICATED CATARACTS. C. HAMBURGER, Brit. J. Ophth. 23: 557 (Aug.) 1939.

Hamburger states that in his opinion persons who have been operated on for glaucoma should not be subjected to a second operation until tentative treatment with drops of glaucosan (synthetic epinephrine) has been tried.

The author states that he is not opposed to any surgical operation for glaucoma simplex. He is convinced, however, of the correctness of the foregoing advice. For those surgeons who fear that an acute attack of glaucoma will develop following the instillation of this drug, massage with it instead of instillation is recommended. Detailed directions are given for this procedure. Quotations from many authors are presented as to the value of the use of this epinephrine substitute in cases of primary and of secondary glaucoma. W. ZENTMAYER.

GLAUCOMA AND THE VEGETATIVE NERVOUS SYSTEM. M. FRADKINA, L. LEVINA, F. STEIN and T. SHUBOVA, Vestnik oftal. 14: 3, 1939.

The authors attempted to establish the relation between the changes occurring in the function of the central nervous system and glaucoma, particularly in cases of unilateral glaucoma or in cases in which one eye is affected more than the other. The study included: (1) examination of the albumin content in the blisters formed on application of cantharides plaster on symmetric regions of the skin; (2) determination of the dermographic reaction, and (3) determination of the hydrophilic reaction, i. e., the time of disappearance of the wheal formed after intradermal injection of physiologic solution of sodium chloride. On the

side affected with glaucoma the content of albumin was higher, the wheal disappeared sooner, and the dermographic reaction was less marked; in other words, a vegetative asymmetry was observed.

In addition, the determination of the metabolism of sugar and aqueous in glaucomatous patients by functional testing of the sugar tolerance indicated also some changes in the central vegetative nervous system.

The following conclusions were arrived at:

1. The extensive vegetative asymmetry in unilateral glaucoma does not fit in with the conception of segmentary cervical vegetative apparatus.

2. The character of the curves of the sugar and aqueous metabolism in glaucomatous patients indicates a disturbance in the central vegetative nervous system.

3. It is probable that the observed changes in the vegetative nervous system play a definite role in the pathogenesis of glaucoma.

O. SITCHEVSKA.

Injuries

CLINICAL AND EXPERIMENTAL STUDIES OF THE OCULAR CHANGES PRODUCED BY CATERPILLAR HAIRS. C. KINUKAWA and S. MATSUDA, Arch. f. Ophth. 140: 70 (Feb.) 1939.

One case of caterpillar ophthalmia in a boy 16 years of age is reported. A caterpillar of the species Gastropache pini had been thrown against his eye. Immediately afterward the eye became severely inflamed. Ophthalmologic examination revealed several caterpillar hairs more or less firmly embedded in the bulbar conjunctiva, cornea and sclera. Most of these hairs were removed. Two weeks later the eye was almost pale, but two hairs could be seen in the cornea and three in the iris. These hairs slowly migrated backward, during which process phases of severe keratoiritis alternated with quiescent periods. One and a half years after the accident there were two distinct corneal opacities representing former sites of hairs and one nodular, tubercle-like lesion of the iris which still contained a fragment of hair. Ophthalmoscopic examination revealed mild optic neuritis and two white rod-shaped choroidal lesions, 1 to 3 disk diameters long and ¼ disk diameter in width. This picture remained unchanged during two and one-half months of clinical observation. This is the third reported case of changes in the fundus in caterpillar ophthalmia. The authors interpreted the rod-shaped choroidal lesions as the result of lodgment and subsequent encapsulation of caterpillar hairs in the choroid. By throwing caterpillars against the opened (by means of a speculum) eye of rabbits, experimental caterpillar ophthalmia was produced by Kinukawa and Matsuda. The migration of hairs backward could be followed and studied in detail. The hairs reached the retina and choroid either through the vitreous or through the ciliary body. The usual reactive changes occurred around the hairs. In 3 of 12 rabbits with experimental caterpillar ophthalmia, the disk showed mild edema, although no hairs could be found at or near the nerve head. Hairs usually reached the posterior segment within two weeks from the time they had struck the bulbar

surface. The ocular movements provided the kinetic energy for the migration of the hair, the direction of which was determined by the innumerable barbs which each hair was carrying.

<div align="right">P. C. KRONFELD.</div>

Instruments

DESCRIPTION OF A NEW PROPTOMETER. J. R. MUTCH, Brit. J. Ophth. 23:677 (Oct.) 1939.

A new proptometer is described by Mutch which consists of a small metal stand with a central plunger, on the upper part of which is a millimeter scale. To use the instrument, the patient's face must be in a horizontal position. The patient is told to close the eyes and direct them straight ahead, that is, toward the ceiling. The highest point of the cornea as seen through the closed upper eyelid is noted, and the plunger of the instrument is allowed to rest on it. The feet of the instrument are then allowed to drop until the longer foot rests on the lower orbital margin and the shorter one on the upper orbital margin. Any exophthalmos or enophthalmos present can be ascertained by reading the scale. The article is illustrated.

<div align="right">W. ZENTMAYER.</div>

Lacrimal Apparatus

INFANTILE DACRYOCYSTITIS TREATED BY SURGICAL DIATHERMY. A. M. MacGILLIVRAY, Brit. J. Ophth. 23:630 (Sept.) 1939.

In cases of intractable dacryocystitis in infants, MacGillivray used diathermy, with the current adjusted to an adequate cauterizing strength. With the patient under chloroform anesthesia the sac is laid bare, as in extirpation of the sac, the incision passing through the fistula. The wound is packed with a pledget of wool soaked with epinephrine hydrochloride. The indifferent electrode is placed under the bare buttocks of the child. The current is sent through a blunt-pointed probe. After removal of the pledget the interior of the sac is thoroughly cauterized, including the infundibulum and the entrance of the nasal duct into the nose. The divided halves of the fistula are cauterized. No stitches are required. The wound heals by granulation.

<div align="right">W. ZENTMAYER.</div>

Lens

EXPERIMENTAL DINITROPHENOL CATARACT. G. BASILE, Ann. di ottal. e clin. ocul. 67:223 (March) 1939.

The author administered dinitrophenol to 15 rabbits in doses varying from 4 to 30 mg. per kilogram of body weight per day. The animals lived from one week to six months. All except those receiving the largest doses, which died within a relatively short time, showed a decrease in weight. None showed any lenticular changes or other changes in the eyes, except for a slight accentuation of the posterior suture lines in 1 animal.

<div align="right">S. R. GIFFORD.</div>

PATHOGENESIS AND INVOLUTION OF CATARACT OF DIABETES MELLITUS. M. BÜCKLERS, Klin. Monatsbl. f. Augenh. 102: 465 (April) 1939.

Bücklers described his observations in a case in which changes in the lenticular turbidity were recorded continuously and metabolic tests were made simultaneously. A tabular report indicated the gradual retrogression of the cataract, the sugar content of the urine and blood, the specific gravity of the urine, the water balance and the dose of insulin that was administered. The retrogression of the turbidity of the lens began in the axis and advanced in an irregular manner toward the periphery, but it seemed to be more rapid on the temporal side. The table discloses that the subsidence of the turbidity was already noticeable at a time at which there still existed a considerable metabolic disturbance. One increase in the blood sugar was accompanied by a slight increase in the turbidity of the lens, but a second increase in the sugar content caused no lenticular changes. It cannot be decided whether the decrease in the visual acuity was caused by a lenticular turbidity or by a change in the refractive power during the temporary hyperopia. The author believes that the two processes developed simultaneously. In trying to find an explanation for these two disorders, the author cites the theory advanced by Granström for the development of the diabetic impairment in the refraction and the one advanced by Braun for the pathogenesis of the lenticular turbidities. Both of these authors ascribe great importance to the disturbance in the mineral and water exchanges. The turbidity in the lens as well as the transitory hyperopia are apparently due to a temporary increase in the water content of the lens.

J. A. M. A.

Neurology

REMISSIONS IN MULTIPLE SCLEROSIS. M. R. BROWN and T. J. PUTNAM, Arch. Neurol. & Psychiat. 41: 913 (May) 1939.

This article is particularly interesting for the statistics as to the frequency of occurrence of the principal symptoms and the course of individual symptoms in 133 cases of multiple sclerosis. In general, the authors found that symptoms evidently due to small lesions, such as diplopia, central scotoma or sensory disturbances of one extremity, tend to regress within a few months, whereas symptoms apparently due to large lesions, such as paraplegia, ataxia and mental deterioration, are usually permanent. They conclude that most lesions of multiple sclerosis go through an acute stage, after which a variable number of fibers regain the ability to conduct impulses, some or many fibers permanently losing the power of conductivity in the presence of most large lesions.

R. IRVINE.

A NOTE ON THREE CASES SHOWING "CROCODILE TEARS" AFTER FACIAL PARALYSIS. L. H. SAVIN, Brit. J. Ophth. 23: 479 (July) 1939.

Three cases in which profuse lacrimation in the eye of the side affected by facial palsy are reported. Such tearing may produce a troublesome secondary blepharitis. Two methods of treatment are sug-

gested: excision of the palpebral portion of the lacrimal gland on the affected side and blocking of Meckel's ganglion with alcohol after the Sluder technic.

W. ZENTMAYER.

Ocular Muscles

PARALYSES OF ASSOCIATED MOVEMENTS OF THE EYES: CLINICAL AND PHYSIOPATHOLOGIC STUDY. P. V. MORAX, Ann. d'ocul. 176: 337 (May) 1939.

In the normal state movements of the ocular globes are all associated binocular ones and occur in two principal forms: (1) parallel movements, such as when the eyes are moved in the same direction, that is, horizontal movements to the left and to the right and vertical movements up and down, and (2) nonparallel movements, convergent and divergent.

In pathologic states different functions of seeing can be altered or suppressed; thus are developed the paralyses of associated movements of the eyes, also known under the name of functional paralyses. Parinaud was the first to group the paralyses of associated movements of the eyes, although he was not the first to write on the subject. In a classic monograph he united them and showed their importance and clinical value. He described four kinds of paralysis of associated movement: paralysis of parallel horizontal movements, paralysis of parallel vertical movements, paralysis of convergent movements and paralysis of divergent movements.

This article is divided into numerous sections dealing with: (1) examination of the associated ocular motility, with regard to both voluntary and reflex movements; (2) complete ophthalmologic examination, including study of the oculomotor paralysis, pupillary modifications, retraction of the upper lid, visual disturbances, the cornea, the visual acuity of the fundus, when necessary, and (3) complete neurologic examination.

Under the second main heading is taken up aspects and value of dissociation of voluntary and reflex movements. This subject matter is subdivided and presented under the following topics: complete dissociation, incomplete dissociation, evolution and dissociation in the hypertonic syndromes.

Diagnosis is then taken up, and the last part of the article is devoted to clinical forms of paralysis of sight. These are divided into two groups; voluntary and automatic reflex forms. The first group is subdivided into voluntary paralysis of sight in all directions, paralysis of voluntary vertical movements of the eyes and paralysis of voluntary lateral movements of the eyes. The second group is subdivided into absolute paralysis of sight in all directions, absolute paralysis of vertical movements of the eyes and absolute paralysis of lateral movements.

S. H. McKEE.

Operations

TECHNIC OF CORNEAL TRANSPLANTATION. O. SHERESHEWSKAYA, Vestnik oftal. 14: 77, 1939.

Filatov's technic is used with the following modifications: A broad conjunctival flap is used which covers the whole cornea: this assures

better fixation. The conjunctiva is undermined along all the limbus after the flap is made. This lessens the tension and the danger of prolapse of the vitreous, and also makes it easier to suture the conjunctival wound of the flap. The chief modification concerns the sutures. Three simple sutures are used instead of two double-armed ones. The two side sutures are tied at the beginning, and only the third, the middle one, is left with a loose loop and is tied after the transplant is put in position. This procedure simplifies and hastens the operation and prevents the entanglement of the loose loops.

O. SITCHEVSKA.

Orbit, Eyeball and Accessory Sinuses

FACIAL AND ORBITAL ACTINOMYCOSIS. E. KALT, Bull. Soc. d'opht. de Paris **51**: 167 (March) 1939.

At the age of 13 a girl had multiple abscesses of the right side of the face and jaw which were considered tuberculous. Healing was slow, with dense scar formation. At the age of 16 an abscess appeared at the external canthus of the right orbit. The inflammation was profound, and hyperostosis of the lateral orbital wall was noted. The external rectus muscle was completely paralyzed. The fundus of the eye was normal, but the visual acuity was reduced to ⅓ by haziness of the corneal epithelium. Treatment consisted of the administration of potassium iodide in doses of 5 Gm. per day and ten applications of radium therapy. The Wassermann reaction was negative. A portion of the granuloma was excised for study. Photographs of the patient, a roentgenogram of the orbit showing the hyperostosis and a photomicrograph of the excised tissue showing the organisms are included in the article. Eight treatments of iodoform ionotherapy with a current of 60 milliamperes for ten minutes was beneficial.

L. L. MAYER.

Parasites

OCULAR EULIASIS (OCULAR CONDITION DUE TO LARVAE). VIAL-LEFONT, HARANT and TEMPLE, Ann. d'ocul. **176**: 417 (June) 1939.

The authors had the good fortune to observe 2 cases of this rare condition, ocular euliasis, which has been seldom seen in France.

Under a subtitle "External Ocular Euliasis," 2 personal observations were reported of involvement of the conjunctival and of the lacrimal sac. Under the subtitle "Internal Ocular Euliasis," the effects of the infection on the anterior and posterior parts of the eye are described.

The recognition of larvae in the conjunctival cul-de-sac is of considerable importance, because destruction of the larvae, which is not difficult, is rapidly followed by cure. On the other hand, the presence of larvae in the interior of the globe is a condition of gravity. While the larvae are often visible in the anterior chamber, their observation in the posterior part of the eye may be impossible. Their presence here may cause iritis, iridocyclitis and other lesions of considerable gravity, sometimes necessitating enucleation of the globe. The authors point out that internal euliasis, often due to Hypoderma bovis, is nearly always found in children. An extensive bibliography accompanies the article.

S. H. McKEE.

Pharmacology

ACETYLARSAN AND ITS TOXIC EFFECT ON THE VISUAL APPARATUS. C. STROOBANTS and C. SCHEPENS, Ann. d'ocul. **176**: 519 (July) 1939.

In discussing the pharmacology of arsenical preparations, the author considers first those which have especially general tonic properties and are weak in their action on spirillums. They rarely cause visual accidents. Birch-Hirschfeld reported that though they cause a central scotoma with hemorrhage of the retina, the trouble ceases when the intoxication is arrested. The second group of preparations consisted of those which had strong action on the spirillums.

The disturbances attributed to the use of acetylarsan include a considerable list that the writers have collected from the literature. Among the visual lesions, retinal hemorrhages and also hemorrhages in the vitreous have been observed. There are many reports of inflammation of the optic nerve.

The authors report a case of optic neuritis in detail, giving the symptoms, pathogenesis, causation, prophylaxis and treatment.

A section is devoted to the use of acetylarsan (a French proprietary preparation stated to be the p-oxyacetylamino phenylarsinate of diethylamine) in ocular therapeutics, and the writers cite Hartmann, who treated 1067 patients without a single accident.

A bibliography accompanies the article. S. H. McKEE.

Retina and Optic Nerve

LATE RESULTS IN RETINAL-DETACHMENT OPERATIONS. D. K. PISCHEL, Am. J. Ophth. **22**: 130 (Feb.) 1939.

Remarking that the true value of an operation for retinal detachment can be estimated only by reviewing the results after a period of time, Pischel studied patients who had been operated on at least a year previously. He discusses the results under: reappearance of detachment; degeneration of the macula; atrophy of the retina; optic atrophy; ectasia of the sclera; troublesome hyperphoria, and development of cataract. The following summary is given:

"Of the 63 patients who had been operated upon at least a year previously, 37, or 58 percent, had a successful issue. Of these 37 successful cases, only 32 could be found for reexamination.

"All cases had been operated upon by the Safar method of multiple diathermy puncture. While in the earliest cases only one line of pins had been inserted, in all the later cases double rows of pins had been used, together with transcleral treatment (Larsson) or with bident electrode.

"There were four cases of more than four years' standing, five of more than three years', six of more than two years', and eighteen of more than one year's standing.

"No relapse had occurred in any case which was 'cured' for three months.

"Four patients 'cured' had a recurrence within three months of the first operation, but were permanently cured by a second operation, while a fifth had two recurrences within the same period of time and was cured by a third operation.

"Only one case of cataract developed in previously uninjured lenses.

"Three cases of traumatic complicated cataract showed an increase in density of the lens opacity, as did one of complicated cataract.

"All vision once regained was successfully retained except in three cases of cataract."

W. S. REESE.

THE PROGNOSTIC SIGNIFICANCE OF OPHTHALMOSCOPIC FINDINGS IN CASES OF HIGH SYSTOLIC BLOOD PRESSURE. ROBERT U. GILLAN, Brit. M. J. 1: 609 (March 25) 1939.

This investigation was undertaken to discover whether or not ophthalmoscopic examination might help in the differentiation of cases of high blood pressure from a prognostic point of view. Eighty-three patients with a blood pressure of more than 170 mm. were examined and were observed for a period up to five years. Two points were especially investigated: (1) the state of the retinal blood vessels and (2) the presence of hemorrhages and exudates in the retina.

In addition to the well known signs of arterial degeneration in the retina, the author speaks of two additional features: (1) a haze overlying the arteries at points, especially at the arteriovenous crossings, which obscure the vessels wholly or in part, and (2) attenuation of the arterial blood stream to the point of complete obliteration in some cases and of reduction to a mere thread in others. The author believes that there is no better criterion than the old one that the degree of narrowing of the lumen of the arteries is an index of the stage to which arterial degeneration has progressed. A study of these patients has shown that there is a close relation between the degree of retinal arteriosclerosis and the incidence of death and of cerebral hemorrhage. In the group with advanced obliteration of the vessels, signs of cerebral hemorrhage developed in seven-eighths within an average of two and a half years.

These patients also showed that there was a relation between the degree of sclerosis and the height of the systolic blood pressure. In fact, the degree of vascular degeneration as observed in the retinal blood vessels affords a much more accurate index of the gravity of the condition than the systolic blood pressure itself. Of patients with high systolic blood pressure, those showing advanced narrowing or obliteration of the retinal arteries are the most liable to cerebral hemorrhage.

Deposits were present in the retinas of 22 patients. In 21 of these the exudates appeared as small white dots. They correspond to the type described by Foster Moore (1925) as belonging to the picture of arteriosclerotic retinitis. In 3 of the patients with exudates signs of cerebral hemorrhage developed. This proves that the presence of exudates does not appear to be of such serious prognostic significance as high systolic blood pressure, nor is it comparable to retinal arterial degeneration. None of these patients showed the usual signs of albuminuric retinitis or of diabetic retinitis. This does not argue that high blood pressure has no influence, but it does argue that it is not the sole cause.

Retinal hemorrhages were noted in 6 patients. The hemorrhages seem to bear little relation to the height of the systolic blood pressure and do not of themselves seem to be of serious import.

The author concludes from this study that in cases of high systolic blood pressure the retinal arteries provide a reliable index of the state of the cerebral arteries and furnish an accurate means of foretelling which persons are most liable to vascular accidents of the brain.

ARNOLD KNAPP.

PURE DIABETIC RETROBULBAR NEURITIS: REPORT OF A CASE. F. TERRIEN, E. AZERAD and J. VOISIN, Bull. Soc. d'opht. de Paris 51: 111 (Feb.) 1939.

A man of 45 had rapid and sudden loss of central vision. The visual acuity of the right eye was 0.1 and that of the left eye 0.2. The peripheral fields were normal, but there were bilateral scotomas for colors. General examination gave entirely negative results except for severe diabetes. There was no evidence of an exogenous poisoning. Treatment of the acidosis by diet and insulin, together with daily injections of acetylcholine and vitamin B, occasioned prompt recovery. On questioning the patient it was found that he had had a similar attack some six months previously due to indiscretion in the diabetic regimen. Few instances of such a toxicity had been reported in the literature. The knowledge that diabetic persons may have involvement of the optic nerves is emphasized by the report of this case.   L. L. MAYER.

LEBER'S DISEASE CURED BY NEUROSURGICAL INTERVENTION. P. PUECH, R. BONNET and L. GUILLAUMAT, Bull. Soc. d'opht. de Paris 51: 116 (Feb.) 1939.

After an attack of whooping cough, a man aged 28 noted loss of vision. A diagnosis of retrobulbar neuritis was made. Various medications were tried without avail. Visual acuity was recorded as 1/50 for each eye with large absolute central scotomas. The retinal arteries gradually became attenuated and the veins somewhat engorged. Inquiry into family history revealed that the mother had Leber's disease; an uncle, the mother's brother, also had a similar condition. At operation serous meningitis of the frontal lobe in the neighborhood of the sylvian fissure was found and in addition arachnoiditis of the area of the optic chiasm.

Excellent drawings of the areas exposed at operation are included. Visual acuity increased to 10/10 in each eye after operation.

L. L. MAYER.

FORMATION OF ANEURYSMAL DILATATIONS OF THE RETINAL ARTERIES IN A PATIENT WITH HYPERTENSION. P. BAILLIART, SCHIFF-WERTHEIMER and L. JUVANON, Bull. Soc. d'opht. de Paris 51: 164 (March) 1939.

Visual difficulties had existed for six months in the left eye of a man 48 years of age. For a year he was known to have general hypertension with the systolic blood pressure ranging between 140 and 220

mm. of mercury. Ocular tension was normal. Vision was 0.2 in the left eye and 1.0 in the right. General examination revealed nothing of significance. Lesions of the arterioles were noted in both retinas. In the right eye the inferior temporal artery appeared as a white cord, and small hemorrhages were found in the neighborhood of the arterioles. Lesions in the left eye were similar but more marked. The arterial tension was raised to 90. Periodic examinations of the left fundus showed progressive formation of arterial aneurysms, which became more readily viewed when pressure was exerted on the globe. The authors believe the condition to be one of arteriolar weakness. Two excellent photographs are shown.

L. L. MAYER.

Trachoma

TRACHOMA AND THE COMPENSATION LAW. A. TISCORNIA and J. M. VILLA ORTIZ, Ann. d'ocul. **176:** 451 (June) 1939.

In a recent article by one of the authors, it was shown that while from the point of view of compensation the proportion of traumatic lesions of the conjunctiva is not large, it is certain nevertheless that a good number of persons with such lesions need the attention of a physician. Post-traumatic conjunctivitis often causes incapacity for work, and ocular disturbances also arise from foreign bodies, subconjunctival hemorrhages, irritated pterygia, steam or chemical burns and trachoma.

Despite the organized efforts against trachoma, this condition still constitutes a great problem. Ocular accidents among trachomatous patients increase relatively with increased industrial activity. Such cases are particularly frequent in certain provinces during the time of the harvest.

Numerous phases of the compensation law with reference to accidents among trachomatous patients are discussed.

An extensive bibliography accompanies the article.

S. H. McKEE.

Tumors

THERAPEUTIC RESULTS IN ONE HUNDRED CASES OF EPITHELIOMA OF THE LID TREATED BY IRRADIATION AT THE RADIUM INSTITUTE OF PARIS BETWEEN 1935 AND 1937. M. A. DOLLFUS, Bull. Soc. d'opht. de Paris **51:** 27 (Jan.) 1939.

Of 100 paitents with epithelioma of the lid, 38 were treated in 1935, 32 in 1936 and 30 in 1937. Thirty-six of the growths were found at the internal canthus, 26 at the interior of the lid, 13 contiguous with the nose, 9 under the orbit, 8 above the orbit and in the region of the eyebrow, 3 on the upper lid, 3 at the corneal limbus, 2 at the external angle and 1 in the orbital cavity. Fifty-seven of the patients were women and 43 men. Radium was used in 96 cases, roentgen ray with radium in 3 cases and teleradium therapy for an enormous epithelioma of the orbit. The technic is explained in full, and the methods used to guard against injury to the eye from the rays are detailed. Eighty-eight patients were considered cured. Complications existing in the eye or its adnexa did not entitle 10 of the patients to be registered as cured.

Extension of the initial lesion in 2 patients could not be halted. With proper care and protection of the eyeball, radiation is preferred to operation because of less chance of ugly scar formation. L. L. MAYER.

UNILATERAL EXOPHTHALMOS OCCASIONED BY A TUMOR OF THE ORBIT METASTASIZING FROM A LATENT CANCER OF THE PROSTATE. P. BONNET and L. PAUFIQUE, Bull. Soc. d'opht. de Paris 51: 63 (Jan.) 1939.

A year previous to this report one of the authors presented a case of tumor of the orbit in which total exenteration was done. The tumor was thought to be primary, but histologic examination revealed its metastatic nature. General examination of the patient showed the existence of a cancer of the prostate. This was confirmed at autopsy by microscopic examination. The present report was enhanced in value by this previous experience. A man of 65 had exophthalmos of the left eye. The condition began a year previously with ptosis, followed in one month by mild proptosis. Pain was rather severe. Movement was possible in all directions, but limited. Its rapid growth was suggestive of malignancy. The results of a general examination, except for the prostate, were negative. A portion of the orbital tumor was removed for diagnosis, and the histologic structure of a prostatic carcinoma was found. The finding of the orbital tumor emphasized the necessity of examining the prostate and also brought out the diagnosis of an asymptomatic malignant growth of the prostate.

L. L. MAYER.

Vision

NUTRITION AND NIGHT BLINDNESS. I. A. MANVILLE, Northwest Med. 38: 208 (June) 1939.

According to Manville, night blindness occurs not only in persons suffering with vitamin A deficiency but in those with diseases of the eye such as glaucoma, choroiditis, optic neuritis, toxic amblyopia, pigmented retinitis and detachment of the retina. He presents the results obtained by various investigators in the measurement of night blindness, and from these figures it is seen that from 20 to 40 per cent of the population are suffering from various degrees of night blindness. Much has been said about night blindness as a cause of accidents, and the author mentions another important phase in relation to the increasing number of traffic accidents. This has to do with the pedestrian and not with the driver. Observations in Portland indicate that a large majority of pedestrians killed by automobiles are 50 years of age or older. It is just as likely, or even more probable, that a person in this age group, in contrast to drivers as a group, will be suffering from vitamin A deficiency and consequently night blindness. Certainly cirrhosis of the liver and perhaps other pathologic changes occurring in the liver among the aged is of far greater frequency than among younger persons. This would predispose to a vitamin A deficiency. J. A. M. A.

Therapeutics

RETROBULBAR NEURITIS AMELIORATED BY PHENOLIZATION OF THE NASAL GANGLION. C. DEJEAN, J. FERRIE and J. ROUX, Arch. Soc. d. sc. méd. et biol. de Montpellier 20: 58 (Feb.) 1939.

In a case in which a presumptive diagnosis of tobacco amblyopia was made the vision on first consultation was 20/200 in the right eye and 16/200 in the left eye. The sinuses were normal except for possible involvement of the posterior ethmoid sinuses. A tampon soaked in Bonain's liquid (equal parts of cocaine hydrochloride, menthol and phenol) was placed in contact with each nasal ganglion for forty minutes. Though the patient continued to smoke and drink (contrary to instructions), the vision improved day by day, and in two weeks it was 20/20 in each eye. The absolute central scotoma disappeared, though red in the central field was seen as orange.

J. E. LEBENSOHN.

VITAMIN A AND EPITHELIZATION OF THE CILIARY LAYER. L. GENET, Bull. Soc. d'opht. de Paris 51: 157 (Feb.) 1939.

Genet reports the beneficial effects of the use of ointment containing vitamin A after removal of an epithelioma of the lacrimal sac. Ordinarily in elderly persons the epithelium may form an epidermoid cyst, which necessitates surgical intervention. With the use of the ointment, healing was without incident in 2 patients.

L. L. MAYER.

MODERN NUTRITION. W. HEUPKE, Klin. Monatsbl. f. Augenh. 102: 161 (Feb.) 1939.

Valuable questions on nutrition in divers climates are discussed with reference to general health and the eyes. The merits of carbohydrates, meat, fish and vegetables are evaluated on this basis for the healthy and the pathologic organism. The prescribing and preparation of a salt-poor diet are given ample space and are illustrated by tables. The author comments on the confirmed value of the raw diet. Furthermore, he discusses physicomedical adjuvants, including baths with carbonic acid, massage of the skin and the administration of potassium nitrate and theobromine combined with the use of glyceryl trinitrate internally. Instructive dietary suggestions are given for the treatment of tuberculosis, with especial mention of the diet outlined for lupus by Sauerbruch and Herrmannsdorfer. Heupke concludes by stressing the importance given to diet in recent years after a long period of disregard. The results of local treatment of and surgical procedures on the eyes may be improved by attention to dietary measures.

K. L. STOLL.

Society Transactions

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

FRANCIS HEED ADLER, M.D., *Chairman*

WARREN S. REESE, M.D., *Clerk*

Feb. 15, 1940

Aplasia of the Optic Nerve. DR. HAROLD G. SCHEIE and DR. A. M. ORNSTEEN.

The literature on aplasia of the optic nerve has been reviewed. Complete aplasia of the optic nerve is due to failure of development of the mesodermal and ectodermal elements, with the result that there is no evidence of an optic papilla in the eye. Hypoplasia of the optic nerve, in which central vessels are present in a small pale disk, is due to absence of the ganglion cell layer of the retina with resulting absence of nerve fibers in the optic nerve. The latter condition was observed in a 3 year old boy who had been blind since birth.

DISCUSSION

DR. MARY BUCHANAN: I had 1 case last year in which both eyes were affected. The disks were very small and gray, and the vessels were extremely narrow. The mother of the patient stated that when she was six months' pregnant she had uremia and was admitted to the hospital for hypertension. Her child, as in the case reported here, was born at full term and is very bright. He is now at the Overlook School for the Blind.

DR. FRANCIS HEED ADLER: If the aplasia of the disk in this case had been due to failure of the ganglion cells to send fibers into the porous optic nerve, it should be possible with red-free illumination to detect absence of the fibers. I tried this but was unsuccessful owing to the difficulty of examination without an anesthetic. Although no fibers were seen, the examination was unsatisfactory, and I cannot say definitely that fibers were absent.

Retinochoroiditis of the Jensen Type with Secondary Glaucoma. DR. THOMAS H. COWAN.

A white woman 34 years of age presented an ocular condition that was diagnosed retinochoroiditis. The lesion, situated near to but not contiguous with the disk, had a whitish, smooth, raised appearance. There were no opacities of the vitreous or signs of uveitis in the anterior segment of the globe. Secondary glaucoma with high tension was present. The only relevant clinical finding was an abscess about a tooth, which later was extracted. The appearance of the lesion gradually changed until it resembled the usual lesion of retinochoroiditis of limited extent, and the tension returned to normal.

Finally, the lesion healed completely, leaving a small, whitish, lightly pigmented scar. Vision equaled 6/6 +. The visual field showed a sector scotoma from a point near the blindspot corresponding to the site of the lesion to the nasal periphery.

DISCUSSION

Dr. WALTER I. LILLIE: Dr. Cowan's case presented two interesting clinical problems:

1. In view of the localized elevated grayish white area in the choroid just temporal and superior to the right optic disk without evidence of any associated inflammation, could the condition have been an early choroidal tumor? This diagnosis was ruled out because of the precipitous onset of the symptoms and the progressive course of the disease, with subsequent regression of all the inflammatory signs except the permanent chorioretinal defect.

2. Should the final diagnosis be Jensen's retinitis or posterior uveitis complicated with a secondary glaucoma?

When I examined this patient the cornea was steamy and thick, and numerous discrete deposits were seen on the posterior corneal surface. The pupil was contracted, and the media were so cloudy that a detailed view of the fundus was impossible. The intraocular tension was 72 mm. of mercury with the Schiötz tonometer. I made a diagnosis of posterior uveitis with secondary glaucoma and advised the use of atropine instead of myotics.

The subsequent course, as described by Dr. Cowan, substantiates this diagnosis, as in my experience secondary glaucoma or uveitis has never been associated with Jensen's retinitis. Also, the final defect of the visual field is not continuous with the physiologic blindspot. These three findings, uveitis, secondary glaucoma and the field defect, are much more typical of uveitis than of Jensen's retinitis.

Dr. THOMAS COWAN: The question of classification of various types of choroiditis is, of course, open to discussion. I do not think that this case is one of true juxtapapillaris, but the definition of Jensen's disease is more or less arbitrary. Recent authors have considered that Jensen's disease can be so diagnosed only when the lesion is contiguous with the disk, although authors directly after the time of Jensen did not conform entirely with this definition and reported cases in which the lesion was far from the disk as belonging to the same category. Heath, a recent writer on the subject, thinks that all those cases in which the lesion is solitary and deep extends far into the retina are related and that the symptoms can be considered typical of a disease which characteristically occurs in young persons under 35 years who are usually intelligent and present no other signs of ill health until the ocular lesion occurs. Many cases of choroiditis of this and of other types have been described in which secondary glaucoma occurred.

I might say that the only case of Jensen's retinochoroiditis in which a pathologic report was made, that of Abraham, was one in which the eye was removed because the lesion was thought to be a tumor. The lesion might be considered a tumor, especially in those instances in which some pigmentation was present in the early stages.

External Exudative Retinitis; Coats's Disease. DR. WILLARD G. MENGEL.

The retinal involvement in this disease is characterized by large masses of white or yellow-white exudate beneath the retinal vessels, associated with cholesterol crystals. The onset is insidious and the causation obscure. The disease occurs in young persons whose general health is excellent. Usually the condition is unilateral.

Two cases were observed. In the first case, that of a woman aged 33, the right eye showed large white areas with cholesterol crystals beneath the inferior temporal and nasal vessels and also extending across the upper part of the fundus beneath the retinal vessels. In this case the associated factors which might be responsible for the exudative retinitis were a sensitivity to tuberculosis and the effect of a miscarriage three months previous to the discovery of blurred vision, with the possibility of small emboli lodging in the retinal vessels.

In the second case, that of a girl aged 2 years, the left eye showed a large white area with cholesterol crystals in the macular region extending between the superior and the inferior temporal blood vessels and laterally from the nerve head to the far temporal periphery. The retinal vessels were clearly visible over the area and were not covered by exudate at any place. The associated factors in this case were repeated trauma and the possible congenital nature of the condition, the result of bleeding in the mother during late pregnancy. These associated factors were present, but proof of a direct connection to the exudative condition could not be made.

DISCUSSION

DR. SIDNEY L. OLSHO: I shall describe the visual fields and retinal picture of a patient with exudative retinitis (case reported in 1929) who was seen also by Dr. Heed. The family history seems significant because it included cases of tuberculosis, disease of the nerve tissues, retinal disease and blindness, with syphilis excluded.

R. G., white, aged 19, was in good health. Her mother died at 36 years of age of an undiagnosed tumor of the brain. Two aunts and the maternal grandmother died of tuberculosis. The patient's father died at the age of 74 of a stroke. His sister, blind, died as a young adult. She was the mother of a child born blind who died in early infancy. Several children of a paternal uncle died while young. The patient has 2 brothers and 4 sisters in good health. One sister, fifteen years older, has poor vision due to retinitis pigmentosa discovered at the age of 9.

Friends noticed a peculiar bright gleam from the left eye of the patient about seven months prior to the time she consulted me in the hope of having the poor vision in the left eye remedied by glasses. Physical examination and clinical laboratory studies gave negative results except as follows: The hemoglobin content was 76 per cent with a normal red cell count. There was no leukocytosis; the differential count showed 62 per cent polymorphonuclears. 35 per cent lymphocytes. and 1 per cent each of mononuclears. eosinophils and basophils. The coagulation time was three minutes.

Vision in the right eye was 20/15 + : that in the left eye was 10/200 in a restricted field. but with color perception retained. The external appearance was normal except for a peculiar light gleam from the left

pupil. Tension was normal. The left pupil reacted poorly to light, and the consensual reflex from left to right was poor.

The left nerve head was hazy and poorly defined, except at its upper temporal margin. The lower three fourths of the fundus was seen as a homogeneous, soft, yellowish white opaque surface raised almost uniformly about 1.5 D. Its borders extended from the margin of the disk upward and temporally and upward and nasally almost as far as the eye could see. The upper nasal border, at first straight, developed a number of undulations which were sharply defined from the nearly normal fundus above and presented some ovoid collections and streaks of soft gray pigment slightly below its superior limit.

The massive yellowish white surface was uniformly of one color. A few lustrous crystalline spots (cholesterol?) were seen in the lower temporal field.

The retinal arteries and veins passed on to the yellowish white area and contrariwise without showing any appreciable bends.

Far down and far out near the 5 o'clock region there was an increased number of good-sized venous and arterial branches, some of which terminated with glomerulus-like coils. In one instance there was an anastomosis of a small vein with an arterial branch. Fusiform swellings were also seen.

The yellowish white surface beyond these vascular coils became billowy and projected several diopters forward in a number of rolls of retinal detachment, in which the ultimate terminal vessels were lost.

Histologic Picture of Secondary Glaucoma. Dr. WILFRED E. FRY.

(This presentation was illustrated with lantern slides.)

One of the most frequent specimens that are sent to the pathologic laboratory is an eye enucleated because of secondary glaucoma. The pathologic material therefore available for the study of secondary glaucoma is large. Changes will occur in all parts of the eye. There are certain conditions which are ordinarily recognized as being frequently associated with secondary glaucoma.

In addition to changes of the eye which are produced by the causes of secondary glaucoma, as shown in this slide, there may be other ocular changes which are recognized as being associated with increased intraocular tension. Of these changes, I want to call praticular attention to two, namely: sclerosis of the iris and ciliary body arterioles and perivascular infiltration of the anterior ciliary vessels. Because of the great number of changes found in either primary or secondary glaucoma, it is difficult to say which bear a causative relation and which are merely secondary to the disease process. Examination of eyes with certain types of secondary glaucoma may be of use, because the eye is frequently enucleated in a relatively early stage of the glaucomatous process instead of in a late stage, as is usually the case when an eye blinded from absolute glaucoma is removed. One of the early signs to which attention has been called is the perivascular infiltration which occurs about the anterior ciliary vessels.

A number of sections of eyes that were enucleated at the University of Pennsylvania were examined. It was possible in most instances to verify the statement of Evans. These sections were of eyes with various conditions and were not limited to those showing intraocular tumor.

The slides presented here were from eyes with intraocular tumor, with one exception. In this instance a melanosarcoma of the iris was present.

The glaucomatous globe may be compared to a sphere which is inflated under pressure. In order to have the pressure maintained in the sphere, not only must any large exit, which might be compared to the canal of Schlemm, be occluded but the sphere must be of nonporous material. In the globe there are many small potential openings at the exit and entrance of vessels and nerves, which, according to the present examination, are occluded by the infiltration of lymphocytes.

<div align="center">DISCUSSION</div>

DR, J. Q. GRIFFITH JR.: I know nothing about glaucoma. It would be rather a simple matter to block such perivascular spaces in animals by injections of kaolin to see if what Dr. Fry would consider secondary glaucoma develops. I believe that a great deal more fluid is absorbed by perivascular and perineural spaces in the central nervous system than is commonly believed. Because there are no quantitative ways of measuring the amount of absorption, either into the blood stream or through these spaces, the general supposition has been that most fluid passes on in the blood vessels. There are methods for blocking "lymphatic absorption" or absorption in the perivascular and perineural spaces. One can perhaps find how important this is by finding out what damage has been done by blocking it. I think this would be a good approach to the problem that Dr. Fry has outlined.

Surgical Treatment of Palsy of the Abducens and Trochlear Nerves.
DR. GLEN GREGORY GIBSON.

Selected cases of palsy of the abducens and trochlear nerves were presented to illustrate the various degrees of these conditions and the type of operative correction which proved to be the most satisfactory in overcoming them. The importance of classifying the degree of both the subnormal rotational power of the palsied muscle and the excessive rotational ability of its direct antagonist were emphasized. The secondary rotational changes in the muscles of the normal eye were demonstrated to be of important surgical significance. The status of the sensory correspondence of the two eyes before the onset of the palsy was demonstrated to be of utmost importance in determining the ultimate outcome. Binocular single vision may be hoped for in cases in which binocularity had been well established before the onset of the palsy and in which the surgical procedure is correctly applied to the abnormally acting muscles. Cosmetic improvement is the most that can be expected in those cases in which the palsy antecedes the development of binocular single vision. Bilateral recession of the internal rectus muscles and recession of the internal rectus muscle combined with the Himmelscheimer technic are recommended when the degree of the palsy and the rotational abnormalities warrant these various procedures in the various types of palsy of the abducens nerve. For palsy of the trochlear nerve, recession of the contralateral inferior rectus muscle gives satisfactory results in proper cases. Occasionally the homolateral inferior oblique muscle also may be tenotomized. It also may occasionally be necessary to operate on both the vertical and the horizontal motor muscles at the same time. Encouraging results may be anticipated when the surgical procedure is applied according to the muscular abnormalities.

DISCUSSION

Dr. Edmund B. Spaeth: Dr. Gibson's presentation as well as his excellent results bear out his latest sentence relative to the satisfactory results which can be obtained. With regard to tendon transplantations for palsy of the abducens nerve, the external rotation which is obtained is not the direct result of the transplantations themselves. The superior and inferior rectus muscles cannot develop any external rotational effect. I think the two transplantations simply increase and augment an aponeurosis along the external rectus muscle at its scleral insertion—the superior rectus above, the inferior rectus below and the advanced external rectus between the two—holding the eye in such a position that the superior and inferior oblique muscles acting together function as external rotators, i. e., to give the abduction which occurs. I am almost sure of this because I saw a startling demonstration of it at the Graduate School of the University of Pennsylvania in the laboratory for work on muscles, where these various isolated palsies are studied as to the diplopia, the head tiltings which occur, etc., by injections into the muscles of healthy persons. A patient following tendon transplantations exhibited 18 to 20 degrees of external rotation. An injection was made along the line of the inferior oblique tendon. The patient immediately lost temporarily all of the external rotation which he had had before the injection. So I am rather certain that the tendon transplantations serve to hold the eye in that position to which it has been moved by the resection of the external rectus muscle and the recession of the internal rectus muscle, and the two oblique muscles together in this position of relative abduction now permit further external rotation.

Just a few words about the mechanics of the surgical treatment of palsy of the trochlear nerve. The operation can be done on either the inferior oblique muscle of the same eye or the inferior rectus muscle of the opposite eye. The indications for surgical intervention are quite definite. Bielschowsky, and White and Duane, separately, have presented indications and contraindications for these two procedures. They feel that tenotomy or resection of the inferior rectus muscle of the contralateral eye is indicated in those cases in which the lateral deviation is least outstanding, or one with esophoria or esotropia, and in those cases of palsy of the trochlear nerve in which overaction is the greatest factor. Bielschowsky was definite in outlining the operation for this. He felt that the subconjunctival recession should be done in the depths of the cul-de-sac, a suture passed through the muscle mass and this then detached from the sclera. One half of the suture is passed through the bulbar conjunctiva and the episcleral tissue beneath the limbus, and then the patient is directed to look from eyes front to eyes laterally, e. g., toward the contralateral direction, and the suture is tied with the eyes in that position while, and at the time the two eyes are horizontally parallel. Tenotomy of the inferior oblique muscle on the same side is to be carried out in those cases in which there is either an accompanying exophoria or in which there is little if any torticollis and little if any overreaction of the contralateral synergist. White feels that the tenotomy of the inferior oblique muscle is an unsatisfactory procedure and is to be done as an operation secondary to that on the inferior rectus muscle on the contralateral side and never as a primary procedure.

NEW YORK ACADEMY OF MEDICINE, SECTION
OF OPHTHALMALOGY

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A Self-Setting Crossed Cylinder. DR. JOSEPH I. PASCAL.

A crossed cylinder set in a mount having its own axis scale makes it possible for the cylinder to be accurately adjusted for any position and kept in that position during the process of twirling. It also has an automatic stop, so that the rotation is exactly through an angle of 180 degrees and provides for rapidly changing the power of the crossed cylinder used. The spherical element can be changed without disturbing the crossed cylinder during the three position test until astigmatism is either uncovered or ruled out. For locating the accurate axis, the axes of the mounted crossed cylinder can be set at 45 degrees to the test cylinder axes and twirled while fixed in the position more easily and more accurately than can be done with a loosely held crossed cylinder.

The Intramarginal Suture in Repair of the Lid. DR. HENRY MINSKY.

Two simple methods of suturing recent lacerations of the borders of the lids follow:

The intramarginal splinting suture consists in forcing a torn border of the lid up against the other intact one by means of a double-armed suture, which is made to pass first in the plane of the gray line by precise placement of equal quadrant arcs through the tips of the wound. Then the lips of the marginal tear are brought together by the first half of a surgeon's knot in order to approximate accurately not only the edges of the torn border but the corresponding parts of the lacerated conjunctiva, which at this stage is repaired by buried interrupted catgut sutures. This mattress suture is finally brought through the plane of the gray line of the intact opposite lid and tied over a rubber bolster, completing the splinting mechanism.

When both lids are involved, this suture takes the form of a figure eight. The correction of a notch may be achieved by the same procedure.

Unusual Lens Changes Following Trauma: Origin and Treatment. DR. DANIEL M. ROLETT.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

Pseudotumor of the Orbit. DR. WILLIS KNIGHTON.

A patient with a unilateral orbital mass associated with exophthalmos and ptosis received six weeks of conservative treatment, after which the mass receded and the exophthalmos disappeared. At the end of

another two weeks no mass could be felt and the eye appeared normal in all respects. A diagnosis of inflammatory pseudotumor of the orbit was made.

DISCUSSION

DR. BYRON SMITH: An Italian 55 years of age with a condition similar to that described by Dr. Knighton was recently treated at the New York Eye and Ear Infirmary in the ophthalmic service of Dr. Bernard Samuels. He first came under observation about three months ago, at which time he complained of lacrimation and progressive exophthalmos. Detailed examination, including roentgenograms of the sinuses, orbit and skull, in addition to a blood test and other laboratory procedures, failed to establish the diagnosis. Exophthalmometer readings over the following two months revealed a slight increase in the degree of unilateral exophthalmos. The visual acuity began to fail, and immobility of the proptosed eye became marked. The opposite eye also suffered a corresponding decrease in visual acuity and an altitudinal defect in the visual field of both eyes. Retinal hemorrhages and edema of the disk developed along with the progress of exophthalmos in the affected eye. About two weeks ago it was decided that an exploration of the orbit should be performed. In view of the fact that deep palpation in the superior nasal quadrant revealed the presence of a dense resistance rather deep in the orbit, it was considered that this region should be chosen as the optimal position for surgical approach. An incision was made through the conjunctiva between the medial rectus and the superior rectus tendon. The superior rectus tendon was dissected free from the globe and the dissection carried toward the apex of the orbit within Tenon's capsule. By this exposure a firm, smooth, rounded, adherent mass was palpated adjacent to the superior nasal quadrant of the orbital wall. A biopsy of the mass was performed with some difficulty due to excessive bleeding. No attempt was made to excise the mass. The postoperative course was uneventful. By microscopic examination the tissue removed from this mass was diagnosed as chronic inflammatory fibrous connective tissue. In view of the bilateral superior altitudinal defect of the visual field, it was considered advisable to carry out further neurologic investigation. A complete neurologic examination indicated nothing more than could be interpreted from the visual fields. At present the patient is under observation at the Neurological Institute for the consideration of encephalography.

Intravital Color of the Macula. DR. JOHAN W. NORDENSON.

The macula of the dead eye is yellow and has for a long time been called the yellow spot. The macula of the living eye has also been thought to be yellow, and on that assumption the explanation of various physiologic optical phenomena have been based.

After the invention of the ophthalmoscope, a yellow color of the macula was sought for in vain, and finally Schweigger (1870) announced that it did not exist in the living retina. Against this assertion, Schmidt-Rimpler advanced the opinion that the yellow color could not be seen until after death, when the retina became opaque and the yellow color became a coating color.

In 1902 Gullstrand undertook a thorough investigation of the question, and as a result stated that no yellow color was to be found in the living retina. The following arguments were advanced in support of this statement: 1. If the retina is carefully dissected from the choroid, no yellow color can be seen in the macula. 2. On ophthalmoscopic examination of richly pigmented eyes, in which much light is reflected from the retinal pigment, and of eyes with an embolus of the central artery of the retina, in which the retina is opaque, and on examination of eyes with the red-free light of the mercury lamp, which is an accurate detector of any yellow color, no yellow light can be seen. 3. The entoptical phenomena in the macula cannot be explained by a yellow color of the same. 4. Likewise, the differences in the central and paracentral color vision speak against the presence of a yellow color in the macula.

The dissections were repeated by Dimmer, Sattler, Schmidt-Rimpler and others, who all found a yellow macula. The ophthalmoscopic examinations were repeated by Dimmer, who corroborated Gullstrand's findings in richly pigmented eyes with the mercury lamp but who was able to see with sunlight a yellow area around the fovea of one-third the diameter of the papilla . He assumed that in the living eye the yellow color was limited to this small area but that after death it diffused into the whole macula.

Gullstrand for his part maintained that on careful dissection the macula did not show any yellow color. He considered that the yellow color seen in sunlight came from the choroid, and he thought it inconceivable that a color that was seen brilliant when occupying a thirty times larger volume in the dead eye should not be seen in the living eye.

The question was then taken up by Vogt. He examined the eye with a red-free light and found, like Dimmer, a smaller yellow spot, which he first, in accordance with Gullstrand, considered as caused by light from the choroid. Later he altered his opinion and declared it to be a color in the retina. He attributed Gullstrand's failure to see this yellow color to weak illumination.

Gullstrand replied that if the darker spot in the center of the macula could be seen only with weak illumination, the light from the surrounding retina was above the threshold of perception, but that as to the yellow light seen by Vogt, no yellow color could be seen in the center with strong illumination. He showed by several arguments that it must be generated by light reflected from the sclera and having its yellow color from the choroid. He also showed that the illumination necessary to give the yellow color was about forty times the illumination necessary for the light to be above the threshold of perception.

To this Vogt replied that it had not been proved that because the light was above the threshold of vision it was also above the threshold for color and that in cases in which the retina was atrophic, no yellow color could be seen in the periphery.

The ophthalmic world having in general accepted the views of Vogt, the work on this subject was taken up later along different lines in the clinic with which I am associated.

The dissections have been repeated by Kugelberg, with the same results that were obtained by Gullstrand. An analysis of the color substance has shown that it is not a carotene.

Ophthalmoscopic observations have shown that when the central dark spot is visible in weak illumination, the light from the surrounding part of the retina is above the threshold for yellow. Further ophthalmoscopic examination of fundi in eyes shortly after death showed no yellow color in the macula. Finally, ophthalmoscopic examination of the periphery of the fundus in red-free light showed that where the retina is as thin as in the fovea a yellow color is to be seen.

Ophthalmoscopic examinations have also been made by Kugelberg in monochromatic light with the aid of a specially built monochromator. With a light which is the contrast color of the yellow in question, one would expect to get a black spot on the macula, but this is not the case. With monochromatic light the light in the yellow area has the same character as the light coming from the tissues behind the retina.

Renewed researches on color mixing undertaken by Olsson with Gullstrand's color mixing apparatus confirmed the opinion that the difference in color vision centrally and paracentrally cannot be explained by an absorption in a yellow color centrally.

In focal illumination of the retina with Koeppe's method in red-free light, no yellow color could be seen, as Koeppe had previously stated.

All these observations tend to make it most likely that there is no yellow color in the macula. Its presence in the dead eye may be due either to a diffusion of color from retinal pigment and choroid or to the circumstance that a colorless substance present in the macula of the living eye by some chemical process suddenly turns yellow.

DISCUSSION

Dr. Ralph I. Lloyd: The yellow color of the macula is easily shown if one will use an adequate source of light (Bausch & Lomb arc light, 1,400 candle power) and filter the rays through a glass cell with an inside depth of 10 mm. and containing a solution of copper sulfate (30 per cent) and eiro-viridin blue (1 per cent). Whether this proves the actual color of the macula or not is beyond me, but it is the only way that I have found what Holm (*Arch. f. Ophth.* 108: 1-85, 1922) says is the real color of the macula. The Hildreth mercury vapor light adapted to the binocular ophthalmoscope of Gullstrand and the white light supplied with that instrument do not give this color at all. No hand ophthalmoscope that I have used has ever shown it either. The only hand ophthalmoscope used in this country that I have not tried for this purpose is the Friedenwald instrument. I have tried Wratten filters of gelatin placed between glass disks and the arc light just described, and the color does not appear. My object in trying out these various devices was not primarily to find the yellow macula but to find the most efficient light to demonstrate retinal lesions in and about the macula. I have also used the sodium light, which shows well any tags of remnants of the hyaloid artery or Bergmeister's papilla attached to the disk and is not uncomfortable to the patient, but it also does not show the yellow color of the macula, nor does it show retinal lesions as well as the red-free light obtained with the solution of copper sulfate and eiro-viridin and the arc light.

Dr. Arnold Knapp: Dr. Nordenson mentioned briefly some experiments he is making with monochromatic light obtained by the use of a prism, whereby he is able to get any kind of light with which he wants to work. Would he tell more in detail about this apparatus?

Dr. J. W. Nordenson: In reply to Dr. Lloyd's statement, the red-free light is a much better test for yellow than a light which contains red. That is a well known physical fact, and that is the reason why one sees it with the red-free light. The yellow color, however, comes from the choroid and not from the retina.

Dr. Knapp has asked how this monochromatic light is obtained. The instrument is of a type which is produced by Zeiss for technical use and in which some alterations were made. The source of light is an arc lamp, from which the light is thrown on a prism through a slit. The prism gives the spectrum from which the desired light is selected through another slit. Both slits are made small, and very pure monochromatic light is obtained. With its use I can now make differential diagnoses. Thus there is a remarkable difference between arteries and veins. There are wavelengths that make the arteries disappear, probably because of the spectral qualities of the arterial blood, whereas the veins show. The choroidal vessels also disappear with the arteries. It may be recollected that many years ago there was a discussion about the vessels of the caput medusae in glaucoma. They were at that time declared by anatomists and physiologists to be arteries; an analysis of their spectrum had shown a spectrum of oxyhemoglobin. If such vessels are examined with this monochromatic light it will be found that they disappear for the same wavelength as the arteries. They are veins which carry presumably arterial blood; for some reason the blood is not reduced enough, the oxygen remains in the blood and the blood gives the oxyhemoglobin spectrum. Again, small black dots in the fundus may be differentiated, because blood pigment dots disappear at certain wavelengths, which, on the other hand, give a good reaction to ordinary pigment. Much of this is not new, because there are many investigators who have been working with filters, but one can never get the exact light wanted with filters.

Harvey Cushing, M.D. Dr. Bernard Samuels.

This paper was published in full as an obituary in the March issue of the Archives, page 633.

DISCUSSION

Dr. Ralph I. Lloyd: Dr. Samuels' paper is worthy of the man he seeks to honor, and that is a great achievement. I should like to call attention to a report by Dr. Cushing (Experiences with Orbito-Ethmoidal Osteomata Having Intracranial Complications, with Report of Four Cases, *Surg., Gynec & Obst.* 44: 721-742, 1927) which is a classic, not only because it depicts the surgeon's point of view but because it displays the true conception of his obligation to his patients and the high ideal this man set for himself. Four patients with this unusual condition had come under Cushing's care. The first 2 had been successfully operated on but died because of an infection passing from the nose through the opening left in the dura. Cushing then devised a plan of occluding this

opening in the dura by a transplant of fascia from the thigh, and the last 2 patients recovered. Reviewing the 2 cases that turned out so unfavorably, he blamed himself for not having foreseen that an infection was likely to pass through this opening in the dura. It is done in the way one would expect now after reading his "Life of Osler" and deserves a place beside the Hippocratic oath in the medical literature.

Patients often say, "You doctors take this as an every-day matter but remember, this is my wife." This article should be read by the laity to get a proper conception of the professional ideal and by the young doctor for an unforgettable exposition of the honorable traditions of the art.

Dr. ERNEST F. KRUG: I knew Dr. Cushing during his very early years in Cleveland. There was one trait of his that should be mentioned and that is the fact that he never lost interest in any patient he ever had under his care. I have evidence of that in 3 patients of mine on whom he operated. He watched 1 patient for twenty years. That patient finally died in Chicago about six years ago. She came to me regularly, and she saw Dr. Cushing regularly until she died. He told me that he was in almost constant correspondence with the patients on whom he operated. He never allowed them to get out of his reach. I think that shows the character of the man. Those patients were a part of him after they had once come under his observation. and they appreciated it. That is why he was so well liked and so well known everywhere.

Book Reviews

Worth's Squint. By F. Bernard Chavasse, M.D. Price, $8. Pp. 688, with 225 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1939.

This book considers the problem of squint from the point of view of comparative anatomy, embryology and reflex physiology. Thus, the first section on foundations of binocular reactions permits an interesting insight into the problems of relative and absolute rest and also into the changes of the various axes during phylogenetic development. The chapter on the close connection of the primitive reflexes of self preservation and aggression and their influence on the angle gamma, the orbital and visual axes and the extent of binocular fields is followed by a discussion of the physiologic questions of fixation and refixation, accommodation and pupillary reflexes. According to the author, the static anatomic bond between the two eyes and its control by the aforementioned reflexes will be strengthened in the vertebrate line with the increasing acuity of stereoscopic vision and refined with the development of the macula and fovea.

The second section treats the ontogenetic changes of the visual and orbital axes and the reflex development of the child. Two essential factors lead to final coordination: the unconditioned reflexes (inborn, dependent on the passage of time) and the conditioned reflexes (empiristic, dependent on usage). The originally acquired conditioned reflexes may become fixed by continued usage in infancy and in early childhood at a time when they are in a state of "flux" (diminishing flux). The author states that the assumed unconditioned fixity will be maintained for life. In the reviewer's opinion, it would be more appropriate to say that they "may" maintain unconditioned fixity, since some are subject to extinction—like abnormal reflexes after the age of 5 to 8 years. The definition of fusion as "a reflex issue, in appropriate reaction, of stimuli incident bi-retinally" is not fortunate and is rather involved.

The following section on the pathology of binocular anomalies is the most complicated part of the book. The problem of squint is considered from the standpoint of reflex pathology. The complexity of the subject matter and the detailed descriptions are at times distracting. In review, some of the outstanding ideas can be mentioned. Sensory, motor and central obstacles—congenital or acquired—may hinder the normal fusion of stimuli. Immature reflexes especially will be menaced. In early childhood even slight obstacles are apt to produce permanent defects. The site and nature of different types of hindrances in the reflex pathway are treated in subclassifications in separate chapters. Heterophoria is discussed in connection with dissociation by primary obstacles. The chapter on dissociation by primary sensory obstacles covers the ophthalmoplegias, asymmetries and other ophthalmoplegic motor obstacles. In the practically valuable chapter on accommodational squint and other types of squint some credit is given to Worth's work.

Of great theoretic importance are the three chapters of this section dealing with the reactions to dissociation, the inhibitions and the sequelae and the secondary correspondences. The terminology is new in parts and makes the reading rather strenuous, and it is not always simple and expressive, as, for example, "reciprocal proprioception," "inhibition of heteroception" and "inhibitory and exhibitory secondary proprioceptive correspondences." When the reader has overcome this difficulty, however, he is rewarded by a fuller understanding of some of the clinical problems of strabismus in the light of reflex pathology. The subject matter is so involved and complicated that a detailed description would be necessary to convey a full impression of the kaleidoscopic variety of questions treated in this section. In the conclusion the author points out that only an adequate knowledge of the development and pathology of binocular reactions can form a trustworthy basis for the diagnosis and treatment of squint.

The fourth section deals with diagnostic questions. It contains a conclusive description of clinical methods for the diagnosis of deviation and of the state of sensory correspondences and a brief consideration of the diagnosis of the cause of squint. Owing to the fact that squint is a problem of infancy, emphasis is placed mostly on methods applicable to this age (except after-image test).

In the fifth section the author states that treatment of squint must be based on a perfect understanding of the pathogenesis in each individual case. This is one of the statements with which every experienced oculist will agree. In Chavasse's opinion, a great number of therapeutic measures now used for certain incurable stages and sequelae may be omitted, and cure may be obtained with a few simple appropriate measures. Removal or neutralization of the cause of squint and its sequelae as soon as possible and eventually the removal of the deviation are the cornerstones of any treatment for squint. The author chooses critically those methods which are applicable from his own clinical experience. It would be much more convincing if some statistics on which his conclusions are based were given. Without them, many of the statements sound apodictic. Chavasse's statement that transient periodic squint with true projection is the only one cured by training (orthoptics) will arouse most controversy among oculists with different experiences; many objections will also arise from some of his advice in connection with surgical treatment (free tenotomy of both internal rectus muscles without control sutures for alternating squint). He is apparently not in favor of operations on the inferior oblique muscles. Here again it would be desirable to see the results in figures of the operations recommended.

Most of the illustrations in black and white are excellent and instructive. A few, however, do not fulfil their purpose. For example, the principle to show the deviation in different glancing directions seems to be carried too far, since a great number of small pictures concentrated in a small area is somewhat confusing.

It is surprising that this book should originate in England where the greatest advances in orthoptic treatment have been reported in recent years. The title, "Worth's Squint," is misleading, for only a few traces of Worth's classic book are evident. Chavasse's book is above all a highly personalized one dominated by the ideas and conclusions of the

author to the almost total exclusion of other references. This characteristic and the original conception of the subject matter make it interesting and, with some restrictions, readable; but it also makes for great subjectivity and immoderation of some of the statements. This is compensated for by the fact that Chavasse is more qualified than other oculists to enlighten some parts of the problem of squint from the standpoint of comparative anatomy, physiology and reflex pathology. Therefore, Chavasse has made an important contribution to a sounder understanding of the fundamental problems of squint.

L. von Sallmann.

Das Antlitz der Blindheit in der Antike: Eine medizinisch-kultur-historische Studie. By A. Albert M. Esser, Dr. med. et phil. Price, 9.50 marks. Pp. 178. Stuttgart: Ferdinand Enke, 1939.

Taken at its face value or, as the French say, *au pied de la lettre,* the title of this monograph would lead the reader to expect a research on the representation of the eye in classical art along the lines of Hugo Magnus' "Das Auge in seinen ästhetischen und culture-geschichtlichen Beziehungen," or of Javal's autobiographic "Entre aveugles." It is, however, something rather different, and far from being a rambling excursion into one of the many interesting by-ways and highways of ophthalmology (Barkan), it offers an erudite, richly documented and inclusive study of blindness in all its aspects, as described, explained and evaluated by contemporary observers, lay and medical, and handed down to posterity by historian, poet and satirist. The field is wide, and the author has explored it deeply. The wealth of citations from Greek and Latin authorities and anthologies, Vedistic tracts and Egyptian papyri deals with the loss (*Blindheit*) and with the destruction (*Erblindung*) of vision with regard to its objective signs, causes and legal and economic implications; with ways and means, mechanical, toxic and, as was believed in classical times, psychic. The chapters devoted to the mental and emotional world of the blind or blinded—they are by no means identical—is particularly complete. There are chapters and verse from many sources on the psychology of blindness, congenital or acquired; on the attitude of the blind person toward the outer, unseen world, in habit, profession and judgment, and, per contra, on the attitude of that outer world toward the blind, as expressed in humanitarian activity and economic support, or, where these were not needed or desired, in sympathetic approval or even veneration. One learns, or rather one is reminded, of blind seers, bards, harpers and singers; of oracles and prophetic souls whose inner vision, embracing the future and the fate of men, more than compensated for the loss of obvious sight.

A curious, and in some respects rather unedifying, section is devoted to the physician, not only in his healing capacity, whether partially or completely successful, but also as a cause of blindness either through carelessness, lack of skill or even criminal intent. This by no means completes the list of topics which Esser has treated exhaustively and, it must be said, a bit exhaustingly. When one considers the vague knowledge of ocular anatomy and physiology, the mystic conception of disease, an empiric therapy based as much on folklore as on factual data, an almost complete ignorance of pathology and, last but not least, a similar lack of

instruments of precision for the examination of the eye in those ages, one cannot but feel that much of the lore handed down is largely conjecture, vague analogy, metaphysical and introspective deliberation; certainly it is not based on scientific interpretation of signs and symptoms and on clinical diagnoses following a thorough examination and based on a knowledge of causes and effects drawn from personal experience and from the teachings of previous trained observers.

Finally one must bear in mind that there is a difference of opinion even as to terminology; no complete agreement as to whether this or that Greek or Arabic term, let alone Egyptian hieroglyph, meant trachoma or cataract or perhaps neither of the two.

The work under consideration treats its subject with characteristic German thoroughness and scholarly equipment but with an equally characteristic tendency to ignore the contributions of previous workers in the same field. This is the more striking in view of the page after page of authors cited from ancient literatures. Their name is legion, and some at least are not familiar to even the fairly well read classicist. This applies as well to the many historical or mythical characters cited as actors in a tragedy, either as blinding or blinded.

To sum up, this is a most interesting and informative monograph for one who perseveres in the study of a mass of detailed lore, although it is made difficult by obscure phraseology and a somewhat labored style.

<div align="right">Percy Fridenberg.</div>

Obituaries

ALFRED BIELSCHOWSKY
1871-1940

Dr. Bielschowsky was born in Namslau, near Breslau, Silesia, on Dec. 11, 1871, and died in New York on Jan. 5, 1940. He was educated in the catholic gymnasium in Glatz and in various German universities. He pursued his ophthalmologic studies in Leipzig, where he was one of five assistants to Sattler, all of whom became prominent professors of ophthalmology and heads of clinics: Carl von Hess, in Marburg, Würtzburg and Munich (Bielschowsky assisted Hess in some of the latter's researches on accommodation); Kruckmann, in Berlin; Bielschowsky, in Marburg and Breslau; Birch-Hirschfeld, in Königsberg, and R. Seefelder, in Innsbruck. In Leipzig, Bielschowsky worked also in the laboratory of Hering, the greatest teacher of visual physiology. Here he was associated with B. F. Hofmann.

This was a truly remarkable environment for the development of an exponent of clinical ophthalmology based on sound physiology and ample clinical material in the stimulating atmosphere of keen associates.

While at Leipzig, Bielschowsky wrote the first paper which he presented before the Deutsche Ophthalmologische Gesellschaft (1897). It was a memorable paper in which he pointed out that stimulation of a single spot in the retina could, in certain persons, cause two sensations with different directional values—monocular diplopia with a single retinal image.

He had been promoted to the assistant professorship at Leipzig when, still a young man in his thirties, he produced his magnum opus in 1907. This was the monograph entitled "Die Motilitätsstörungen der Augen nach dem Stande der neuesten Forschungen." It was contributed to the Graefe-Saemisch "Handbuch der gesamtem Augenheilkunde" and far surpassed all efforts of previous authors laboring in the field of ocular motility, for example, the monograph by Alfred Graefe, senior editor of the "Handbuch."

In 1918, while head of the department of ophthalmology in Marburg, he was made *Geheimrath,* one of the last orders signed by Wilhelm II.

From Marburg, Bielschowsky was promoted to the large clinic at Breslau University. At the time of his death, Dr. Bielschowsky was professor emeritus on leave of absence from the University of Breslau until 1941. It seems significant that in spite of his Semitic blood he was in good standing with the authorities, though I am informed that

there had been some anti-Semitic student demonstrations toward him. Also his name has been dropped from the list of editors of von Graefe's *Archiv für Ophthalmologie* and of the *Zentralblatt für die gesamte Ophthalmologie*.

In 1934, at the invitation of Dr. Arnold Knapp, Dr. Bielschowsky visited the United States and gave a series of lectures in New York, Chicago and half a dozen other cities. While in Boston he was introduced by me to Professor Ames, of Dartmouth. He was invited to spend six months at the Dartmouth Eye Institute. Dr. Bielschowsky accepted and was so impressed that on his return to Germany he obtained a prolonged leave of absence and arranged to make his permanent home in Hanover, N. H. In 1937 he became professor of ophthalmology and director of the Dartmouth Eye Institute. In this congenial atmosphere, engaged in clinical, didactic and research work, with frequent trips to various parts of the country, Bielschowsky spent the happiest years of his life. It is there that he was buried, only a few yards from Eleazer Wheelock, founder of Dartmouth College.

Dr. Bielschowsky's special studies and experience in the field of motor anomalies and the physiology and pathology of binocular vision made him peculiarly fitted to appraise the work of Ames and his coadjutors. Few ophthalmologists could appreciate the researches of the Dartmouth group or give any sound criticism or appraisal of the work. That the one man best fitted to judge gave the work his enthusiastic support was a source of great encouragement and satisfaction to the workers and a valuable guide in the clinical application of their discoveries.

An important part of Dr. Bielschowsky's contribution to ophthalmology was his missionary work in spreading sound instruction on disturbances of ocular motility. He made as many trips as his work at Hanover and the limitations of his health permitted, to all parts of the country from the Atlantic to the Pacific. It was Bielschowsky's custom to devote half or less of the time to a lecture carefully prepared and half or more to the demonstration of cases with discussion of diagnosis and treatment. The demand for reprints of his lectures was so great that a special edition of them was soon exhausted and so were all the copies of the periodicals in which they appeared. A new edition has just been published.

He was returning from such a trip to Los Angeles and other cities when he stopped at his daughter's home in Brooklyn and was taken to the hospital for study and operation. Dr. Bielschowsky suffered a good deal from peptic ulcer and was operated on for perforation in 1923. For some time before his death there had been unmistakable signs of a cerebral (left frontal) lesion, and the immediate cause of his death was a massive hemorrhage following an attempted pneumoencephalography.

A definitive critical estimate of the work of Dr. Bielschowsky is a matter for the future and for more competent judges than me. Is it not clear that the reason Dr. Bielschowsky was able to build so greatly, to

ALFRED BIELSCHOWSKY
1871–1940

write so clear and convincingly and to speak with authority was that he built on the broad and deep foundation of sound physiology? Indeed, he himself points to this in the first paragraph of his monograph

in the Graefe-Saemisch "Handbuch" (1907) in which he proposes to give a "short exposition of those physiologic facts whose mastery is the indispensable prerequisite to an understanding of the pathologic phenomena, to an exact and exhaustive investigation of them as well as to a well directed application of the methods of treatment." It is significant that Graefe had stressed the anatomic and Bielschowsky the physiologic aspects of the subject. Dr. Bielschowsky fully appreciated his debt to Hering. He was one of the few European ophthalmologists who was well informed on American ophthalmic literature.

While the "Handbuch der gesamten Augenheilkunde" was in course of publication, the "American Encyclopedia and Dictionary of Ophthalmology" was published. The article on motility was by Savage. His writings were the most widely read in America. Savage ignored physiology, or rather he invented his own physiology to fit his theories, as do some American writers of prominence today, indifferent to the work of other investigators. Bielschowsky was spreading the doctrine of sound physiology, which in time will crowd out the weeds of false doctrine so widely prevalent in America even yet. To be sure, the country had a few sound teachers, notably Duane; moreover, Stevens was the father of the whole field of heterophoria.. Nevertheless, when Dr. Bielschowsky completed his first tour of the United States in 1934 he was not only disappointed but appalled at the ignorance of American ophthalmologists in the field of binocular vision and ocular motility. It is hoped that there will be a whole crop of teachers on whom his mantle will fall.

Dr. Bielschowsky did a notable piece of work for the blind. Over 3,000 Germans had returned blind from the battlefields. Many of these were university men or men of sufficient intellectual interests and mental qualifications to aspire to an academic education and corresponding profession. To meet their needs, an Association of the Blind Academicians of Germany was formed. With the collaboration of great libraries and professors of the philosophic, biologic, scientific and theologic faculties of the universities, a library in Braille covering these fields, including grammars, dictionaries in various languages, textbooks and classics—any book demanded by a blind student the importance of which was evident—was promptly produced, until now the Marburg scientific library for blind students has over 20,000 folio volumes in Braille. After these students complete their studies, positions are obtained for many of them (for example, positions have been obtained for 6 blind university professors, 44 lawyers and 107 musicians).

Dr. Bielschowsky's bibliography comprises 132 items. He delivered in this country at least 123 lectures besides the papers he read at various medical meetings and staff meetings at the Dartmouth Clinic, to which all ophthalmologists were invited.

Dr. Bielschowsky was:

Coeditor of von Graefe's *Archiv für Ophthalmologie* from 1928 to 1936, when his name was stricken from the list.

Coeditor of *Klinische Monatsblätter für Augenheilkunde* since 1912.

Cofounder and coeditor of the *Zentralblatt für Ophthalmologie*. With the thirty-fourth volume his name disappeared from the title page.

A list of Dr. Bielschowsky's honors and of societies in which he held membership follows:

Hungarian Ophthalmological Society, honorary member, 1929.
Swedish Medical Society, 1937.
Honorary Master of Arts, Dartmouth College, 1937.
Deutsche Ophthalmologische Gesellschaft.
Local German societies.
American Medical Association.
Local, state and county medical societies.
New England Ophthalmological Society.
Association for Research in Ophthalmology.

WALTER B. LANCASTER.

Dr. Alfred Bielschowsky was one of the great figures in ophthalmology whose name will never be forgotten. Yet to those who were so fortunate as to have known him, the memories of what he was as a man crowd out the thoughts of what he accomplished.

Perhaps there is no better way to convey an impression of his personality than to quote the editorial that appeared soon after his death in the *Hanover Gazette* (N. H.), a small town weekly paper. It expresses the feelings of his northern New England neighbors, to whom he came as a stranger—a foreigner—but five short years before:

He came to break bread with us. He was a small man with gray hair, bushy eyebrows, a moustache, and piercing dark eyes. His accent was foreign, his manner mild, his attitude one of humility. He seemed to think we were people of importance and in some way helped us to believe it true. Later we were to learn of his genius and his great service to humankind through the science of ophthalmology. It was our turn to be humble and yet it did not seem necessary in the fellowship that was so much enjoyed.

The personality of a great master of science whose life was dedicated to the relief of human suffering followed a pattern for Christian living. His inspiration to his fellow workers leaves them fortified in their continued efforts to accomplish great things. Why attempt to deny immortality while there are eyes with which to see, and lives to live so meaningfull?

To those who worked closely with Dr. Bielschowsky, he was not only a walking encyclopedia of scientific and clinical information but a counsellor and friend whose breadth of vision and kind wisdom could always be relied on.

The depth of his understanding is exemplified in the following anecdote:

Late one afternoon, soon after he came to Hanover, we were working on a difficult clinical case on which we had obtained most interesting data by a new method of measurement. I did not feel that he grasped the full significance of the data or would go far enough in applying them in diagnosing the condition. In my earnestness, I expressed myself positively and sharply. While thinking it over later, I felt ashamed, and when Dr. Bielschowsky came in the next morning I apologized most humbly. He smiled and put his arm around my shoulder: "Thank you," he said. "I understand perfectly. Let me explain." He then went on to say that his early training was in research but that, because during most of his life he had been engaged in clinical practice, his attitude now was primarily that of a clinician; that a clinician's attitude must be one of faith in accepted knowledge and established procedures, and that he must always be on the defense against new untested ideas. "On the other hand," he said, "you, as a researcher, must have just the opposite attitude; you cannot be satisfied with accepted ideas and procedures; you must find fault with them and always be trying out new possibilities. This difference between us is as it should be, and because of it we will accomplish a great deal working together; also because of it we must have many arguments."

He was really only explaining to me what he had been practicing throughout his life, as is evidenced by his accomplishments. They are an extraordinary integration of research and clinical activities in which, on the one hand, his profound background of knowledge never became so crystallized as to prevent him from seeing new possibilities and, on the other hand, the enthusiasms of his new visions never led him to overvaluate them.

His voluminous published works are perhaps unique to the extent that they show a continually increasing understanding of the basic physiology within his field made applicable to clinical practice.

When a great man dies there is always a loss to mankind, because no one else can do what he could have done had he lived. This loss is particularly great in Dr. Bielschowsky's case. There is no one in the ophthalmologic field with his background in research and breadth of clinical knowledge. And, what is more, there is little promise that such a figure will soon again appear, for today there is no place where one can get the training and background that Dr. Bielschowsky received in his early life.

ADELBERT AMES JR.

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Directory of Ophthalmologic Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6°, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov.
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All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-
   Michel, Paris, 6°, France.

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President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each
   month.

GERMAN OPHTHALMOLOGICAL SOCIETY

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.
Place: Heidelberg. Time: Aug. 5-7, 1940.

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President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria
   ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

MIDLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secreatry: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

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to make this list complete and keep it up to date.

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President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA
President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.
Place: Perth, Western Australia. Time: Sept. 2 and 7, 1940.

OPHTHALMOLOGICAL SOCIETY OF EGYPT
President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Bachler St., Cairo.
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Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY
President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS
Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 4-6, 1940.

PALESTINE OPHTHALMOLOGICAL SOCIETY
President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY
President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY
President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA
President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA
President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE
Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7ᵉ.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS
President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Secretary: Dr. Derrick T. Vail Jr., 441 Vine St., Cincinnati.
Place: New York. Time: June 10-14, 1940.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank E. Brawley, 30 N. Michigan Ave., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts
    Bldg., Omaha.
Place: Cleveland. Time: Oct. 6-11, 1940.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Frederick Tooke, 1482 Mountain St., Montreal, Canada.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va. Time: June 3-5, 1940.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.
Place: New York. Time: June 11, 1940.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.
Place: Royal York Hotel, Toronto. Time: June 19-21, 1940.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.
Executive Director: Mrs. Eleanor Brown Merrill, 50 W. 50th St., New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Andrew Rados, 31 Lincoln Park, Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of
    each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. G. Nadeau, 122 E. Walnut St., Green Bay.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: The Gateway Inn, Land O'Lakes. Time: June 1940.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Edwin B. Goodall, 101 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time:
    8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. Frederick G. Sprowl, 421 Riverside Ave., Spokane, Wash.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: Spokane, Wash. Time: June 24-27, 1940.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence W. Shannon, 4th and Pike Bldg., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1215-4th Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. L. A. Shultz, 303 N. Main St., Rockford, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. Don M. Howell, Alma, Mich.
Secretary-Treasurer: Dr. Louis D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

Sioux Valley Eye and Ear Academy

President: Dr. R. A. Kelly, 304 N. Main St., Mitchell, S. D.
Secretary-Treasurer: Dr. J. C. Decker, 515 Frances Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. Dake Biddle, 123 S. Stone Ave., Tucson, Ariz.
Secretary: Dr. A. E. Cruthirds, 15 E. Monroe St., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. Carl Wencke, Battle Creek.
Secretary-Treasurer: Dr. A. K. Zinn, Battle Creek.
Time: Third Thursday of alternate months.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Hugh B. Barclay, 111 S. Main St., Greensburg.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. Virgil Payne, Pine Bluff.
Secretary-Treasurer: Dr. Raymond C. Cook, 1005 Donaghey Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. Melville Black, 424 Metropolitan Bldg., Denver.
Secretary: Dr. John C. Long, 324 Metropolitan Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. Shirley H. Baron, 309 State St., New London.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. Grady E. Clay, 384 Peachtree St. N. E., Atlanta.
Secretary-Treasurer: Dr. J. Mason Baird, 511 Medical Arts Bldg., Atlanta.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. Marlow W. Manion, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: Indianapolis. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. H. H. Lamb, American Bank Bldg., Davenport.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.
Place: Davenport.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. D. C. Montgomery, 301 Washington Ave., Greenville, Miss.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. O. B. McGillicuddy, 124 W. Allegan St., Lansing.
Secretary: Dr. A. R. McKinney, 330 S. Washington Ave., Saginaw.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. James S. Shipman, 542 Cooper St., Camden.
Secretary: Dr. Wright McMillan, 23 Passaic Ave., Passaic.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Chester C. Cott, 333 Linwood Ave., Buffalo.
Secretary: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. A. G. Woodward, 100 S. James St., Goldsboro.
Secretary-Treasurer: Dr. M. R. Gibson, Professional Bldg., Raleigh.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. S. B. Fishburne, 1430 Marion St., Columbia.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. J. W. Ward, 2607½ Lee St., Greenville.
Secretary: Dr. Dan Brannin, Medical Arts Bldg., Dallas.
Place: Fort Worth. Time: December 1940.

Utah Ophthalmological Society

President: Dr. A. E. Callaghan, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Charles T. St. Clair, 418 Bland St., Bluefield, W. Va.
Secretary-Treasurer: Dr. M. H. Williams, 30½ Franklin Rd. S. W., Roanoke.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. L. E. Brown, Second National Bldg., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Anderson, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. Arthur G. Fort, 478 Peachtree St. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p m., second Wednesday of each month from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Frank B. Walsh, Wilmer Institute, Johns Hopkins Hospital, Baltimore.
Secretary: Dr. Fred M. Reese, 6 E. Eager St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.
Secretary: Dr. N. E. Miles, 408 Medical Arts Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. E. Clifford Place, 59 Livingston St., Brooklyn.
Secretary-Treasurer: Dr. Frank Mallon, 1135 Park Pl., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.
Secretary: Dr. A. H. Benz, 706 Medical Arts Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Earle B. Fowler, 55 E. Washington St., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington, St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI OPHTHALMIC CLUB

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p.m., third Monday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGIC CLUB

Chairman: Dr. Albert J. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. Harry M. Sage, 9 Buttles Ave., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, *289 E. State St., Columbus, Ohio.*
Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Tex.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. E. G. Linn, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Arthur S. Hale, 1609 Eaton Tower, Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. R. A. Gough, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. Charles R. Lees, 806 Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Dewey R. Heetderks, 405 Medical Arts Bldg., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Robert G. Laird, 116 E. Fulton St., Grand Rapids, Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. J. Charles Dickson, 1617 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. C. W. Rutherford, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to June.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. E. N. Robertson, Concordia, Kan.
Secretary: Dr. John S. Knight, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November,
    January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October
    to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time:
    6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, Brown Bldg., Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from
    September to May, inclusive.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Earle Breeding, 1801 I St. N. W., Washington.
Secretary: Dr. Elmer Shepherd, 1606–20th St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from
    October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sonders, Medical Arts Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m.,
    second Tuesday of each month.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from
    October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretray: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Guy Maness, 119–7th Ave., Nashville, Tenn.
Secretary-Treasurer: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from
    October to May.

New Haven Ophthalmological Society

President: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg.   Time: 8 p. m., second Tuesday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. David H. Webster, 140 E. 54th St., New York.
Secretary: Dr. Robert K. Lambert, 10 101–15th Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Arthur M. Yudkin, 257 Church St., New Haven, Conn.
Secretary: Dr. Benjamin Esterman, 515 Park Ave., New York.
Place: Squibb Hall, 745-5th Ave.   Time: 8 p. m., first Monday of each month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. W. Howard Heine, 635 N. Main St., Fremont, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha.   Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President. Dr. R. N. Berke, 430 Union St., Hackensack, N. J.
Secretary-Treasurer: Dr. T. A. Sanfacon, 340 Park Ave., Paterson, N. J.
Place: Paterson Eye and Ear Infirmary.   Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Adolph Krebs, 509 Liberty Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg.   Time: Fourth Monday of each month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club.   Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Edwin S. Ingersoll, 26 S. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave.   Time: 8 p. m., second Wednesday of each month from September to May.

St. Louis Ophthalmic Society

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Oscar H. Judkins, 414 Navarro St., San Antonio, Texas.
Secretary-Treasurer: Dr. Wilfred E. Muldoon, 414 Navarro St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Matthew Hosmer, 384 Post St., San Francisco.
Secretary: Dr. Fred Boyle, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. I. Henry Smith, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Walter W. Henderson, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. James F. Cahill, 428 S. Salina St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. Herbert Katz, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Frank Costenbader, 1726 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. L. Conner Moss, 1710 Rhode Island Ave., N.W., Washington, D. C.
Place: Episcopal Eye and Ear Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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AFTER HALF A CENTURY OF CATARACT EXTRACTION

CHARLES BRAMMAN MEDING, M.D.

NEW YORK

In a syllabus issued by the American Board of Ophthalmology in 1939, practically a copy of a textbook index, cataract extraction is used for the test in ophthalmic surgery. This operation is the most inclusive procedure in ophthalmology, though not the commonest; factually, the majority of ophthalmologists do no extractions. On pages 4 and 16 of the syllabus, the authors' wisdom shines forth in these headings:

Preparation of patient.
Anesthesia in detail.
Asepsis and antisepsis.
Anatomy *applied* [italics mine].
Tissue reaction to surgical injury.
Reasons for technic.
Avoidance of complication.
Handling of complication.
Candidate (surgeon) at his ease.

A résumé of these fundamentals with omission of the infinity of detail and argument which in crucial moments distract attention is seriously offered in this paper to the young in years and experience as a definite and trustworthy guide to the preparation for, and the practice and studious mediation of, cataract extraction. The material offered is the result of fifty years of clinical experience enriched by personal attendance on teachers who gave without reservation. In gratitude and veneration, I mention those I best remember: Agnew, Born, de Schweinitz, de Wecker, Elschnig, Nettleship, Eversbush, Elliot, Fox, Green, Juler Sr., Kalt, Herman and Arnold Knapp, Meller, Peters, Roosa, Colonel Henry Smith, Swineburne, D. T. Vail, John E. Weeks and Worth. Of varying facility in operation, all were or are men of education, high position, wide reading and large experinece. They have all written, and often I quote or paraphrase their gifts of instruction, but all I have learned has been beaten out at my own forge with no one to share success or failure. One may not escape the influence of continued reading or the variations prompted by practice and one may also misinterpret the spoken word, but it is impossible to efface what

the eyes have seen. Argument falls when the premises are unacceptable. Every calculation must heed the variant, and it is well to admit that in surgery there are two, the surgeon and the patient.

In advising books, I mention a few never to be classics, which for my countrymen are usefully replete. They are Norris and Oliver's [1] "System of Diseases of the Eyes," for which Herman Knapp wrote the article on operations [2] and Fuchs's "Text-Book of Ophthalmology." [3] After these are mastered, there are two lesser books, "Symposium on the Extraction of Senile Cataract," [4] by Harry W. Woodruff, and a similar volume [5] by J. Herbert Claiborne, both almost forgotten but rich in helpful instruction. Two working manuals that put steel in the nerve and truth in the judgment are "Cataract Extraction," by H. Herbert, [6] and "The Intracapsular Operation," by Henry Smith. [7] For a condensed review with a marvelous bibliography, I advise making a fast friend of "Cataract: Its Etiology and Treatment," by Clyde and A. Clapp, [8] and also the reading of Bacon [9] "On Studies."

Each generation takes on the work of its progenitors, and thus the old is reborn. All that contributed to yesterday's bequest rises again to halt and guide today's capital. Thus each new ophthalmologist must struggle through the forest of modified modification until he finally emerges into the cleared way of his grandfather. Since accidents and errors are not always final, their victims and perpetrators find ways of refuge, and what was intended slips through via what happened. Thus a new instrument, a new method in expression or support, finding use here and there in like emergencies, suffices six, ten or twenty times and enters the literature. By such pathways, one reaches the mainroads—extracapsular or intracapsular extraction, with or without conjunctival flap or stitch—and, by eliminating the curious and fantastic fruits of overspecialization, achieves proficiency in a major operation for the relief of an age old affliction.

1. Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1897-1898.

2. Knapp, H., in Norris and Oliver,[1] vol. 3, p. 777.

3. Fuchs, E.: Text-Book of Ophthalmology, translated by A. Duane, ed. 6, Philadelphia, J. B. Lippincott Company, 1919.

4. Woodruff, H. W.: Symposium on the Extraction of Senile Cataract, Chicago, Cleveland Press, 1912.

5. Claiborne, J. H.: Cataract Extraction, New York, William Wood & Company, 1908.

6. Herbert, H.: Cataract Extraction, London, Baillière, Tindall & Cox, 1908.

7. Smith, H.: The Intracapsular Operation, in The Treatment of Cataract and Some Other Common Ocular Affections, ed. 2, London, Butterworth & Company, 1928.

8. Clapp, C. A.: Cataract: Its Etiology and Treatment, Philadelphia, Lea & Febiger, 1934.

9. Bacon, F.: On Studies, in Essays, edited by G. Montgomery, New York, The Macmillan Company, 1930.

Few men have performed large numbers of extractions, but it is not necessary to exaggerate performances to glorify either method or surgeon, for the cataract operation is but a happy combination of maneuvers, for each of which there is sufficient demand to give practice, and it is in this way that the necessary skill must be obtained. The surgeon who is well practiced in work on the lids, conjunctiva and the cornea, who is skilful in the daily grind of removing foreign bodies from the eyeball or orbit, who can regulate muscles and deal safely with wounds, who knows his tools and who has a velvet-like touch, wise judgment and experienced courage will do extractions and restore sight.

It is taken for granted in this paper that the reader has operated on the eye and has learned the technic of section, iridectomy, capsulotomy and expression. One may scarcely attain this from books, but having learned it, one may find comfort and assistance from the experience of those who likewise "know how." The eye is the operator's best ally. It will take many beatings and, aside from expulsive hemorrhage, loss of half its contents and virulent infection, will survive much bungling.

Many modifications of extraction are little more than whims. On reading symposiums, one smiles at the large amount of mere print in their content. If the questions "How many?" "For what sort of patient and eye?" "What did you do in each?" "How long before the patients were discharged and with what vision?" were simply answered, one might be informed, but such remarks as "Too many prolapses," "Too much astigmatism," "Too much vitreous," "Too dangerous," "Too difficult" and "I find" help no one.

On examining man's handiwork in arts and crafts, one finds that inaccuracy, carelessness and inaptitude are common afflictions. Scarcely an article of general use can be accepted without rigid inspection, and this one attributes to the human element. In surgery, too, one must be sure that it is not this element rather than the method which dominates. Approaching the subject of cataract extraction professionally, the ophthalmologist declares that the operation is for the restoration of sight. Surgeon, instruments, methods and statistics of accidents, complications, successes and failures all focus for each patient on this objective. Dedicated to so high a mission, the ophthalmologist should be shriven by a mastery of the applied anatomy and pathology of the eye, which are the arbiters of its medication and surgery and a dioristic measure of the eye's continuity with the whole, which elucidates the etiology of its diseases. To this must be added the hippocratian wisdom of "air, water and places" and facility with men and with instruments. The heights cannot be reached save by the ladder of labor.

A fabric shell filled with water and jelly, placed in an open bony socket connected by bands and cords with the distant sources on which it depends for life and function presents for consideration problems of

texture, elasticity, compressibility and repair. These must be met by good sense, good hands and courage and above all with patient persistence, ending only with the completion of the task. The thousands of persons with cataracts unsuccessfully operated on who are making the rounds of clinics do not all do so voluntarily. Cataract may present a life-long problem. Imperative, therefore, is a studied diagnosis and prognosis preceding operation, lest details which later cause complications and even prevent success be neglected.

The majority of patients with cataract have passed middle life; many are old. The importance of preparing persons for two weeks or more of hospitalization brings into consideration their habits, their digestion, the state of their bowels and bladder, their sores and discharges, their hearing and their mental complex. The changes of habitat, loneliness and worry as to the outcome of the operation are all possible factors in producing failure. I remember a woman of 90 who collapsed the day after an uneventful operation. She had lost her home and her money and had suffered a family catastrophe; for ten days she lay as one about to die. The eye did die! A year later the other eye was operated on, but the patient was rested and reinstated; there was a perfect result.

It is not necessary to exaggerate sentiment, but to the ophthalmic surgeon blindness is death. It is unfortunate that so many case histories are silent as to the preoperative conditions, for one great element in eliminating operative failure is a wise understanding of such contraindications as active ocular diseases and their complications. Inflammatory processes increase the dangers of operation, as do purulent conditions in or adjoining the eye; damaged retinas, scarred corneas, iritis, iridocyclitis and degeneration of the macula are contraindications. As to the much stressed importance of the dangers of operating in the presence of such general diseases as diabetes, nephritis, rheumatism, high blood pressure and allergic sensitivity, there is practically no agreement. It is good practice to be informed as to their presence, to reduce the sugar and urea contents and to seek usual intermissions. Cataract extraction for a rheumatic patient is a lottery, yet there is no more reason to refuse a blind person an extraction than an appendectomy. A sane approach to the operation by the prescription of a diet, general abstemiousness and rest is a precursor of success.

The seriousness of dental decay, ordinary conjunctivitis and chronic bronchitis must be matched against the life and habits of the patient. To begin to reform, reeducate and repair a patient on the verge of an operation is stupidity. At times preliminary hospitalization is necessary to give some persons a needed rest; for others, the twenty-four hours before an operation are just twenty-four hours of dread. Why punish them? Procrustean methods are often inhuman. Persons accustomed to alcohol should be humored. Patients' habits as to aperients, purgatives and hypnotics should not be changed. I condemn detailed examina-

tion, multitudinous tests and challenges to the myriad flaws and deficiencies common to age and senility.

After a cataract in one or both eyes is diagnosed, a careful visual test should be made. If the patient is always supplied with a dated copy of the results of this test, further collection of data is pleasantly facilitated. Memory is short. The patients should understand the possibility of succeeding operations, their probable nature and cost. Just what is a cataract extraction? When does it begin? When is it finished and what does it include?

The ophthalmologist should also show a decent interest in the patient's destination after he leaves the hospital, particularly if the operation has been a failure. One should never operate when ignorant of the patient's circumstances. It is inhuman to put a blind person on the street, and extraction is never compulsory. An operation should have definite indications. Senile cataracts generally affect both eyes; usually the vision in one dims first. The patient's practical vision and social status should be noted. Since an aphakic eye cannot be harnessed with a normal eye, it is best not to operate if the patient's usual style of living is unhampered, for only mutual unhappiness can result from an operation which seems useless. It is well to measure the progress of the failing vision in the seeing eye. Often years elapse before an operation is needed. The psychology of the patient with cataract is worth study. Senility has to be reckoned with, but surely nothing can be more despicable than the prolonged treatment of the incipient cataract and a continued prescribing of useless glasses.

Should one operate when both eyes have immature cataracts which are ruining their victim's life? Under such circumstances it is cruel to wait for the cataracts to become mature. The poorer eye should be operated on first; however, both eyes may be operated on at the same time. The objections to bilateral operation are personal. Two eyes can heal as well as one. Possibly the experience of most men has not permitted this conclusion, but the opportunity of performing a bilateral operation will not be frequent enough to make discussion profitable.

After the status quo is appraised, the type of operation should be decided on. Are surgeons equally at home with all types? It is not the difficulty of the operative procedure but the condition of the eye and the facility of the operator, that are important factors. I fear surgeons who are slaves to a single type of operation; it is a good rule, however, to make a decision as to the type and proceed accordingly. For instance, Peters makes it a rule to tell his observers: "In this hospital, we prepare for and intend to perform intracapsular extraction. If we fail, it is because of circumstances over which we find no control." This stamps the type of man. Efficiency and skill are never achieved by following haphazard methods. It is well to be amphidextrous, but since equality

in hands is rare, the patient should be given the benefit of the best hand. One should do as one would be done by.

FUNDAMENTALS OF CATARACT EXTRACTION

All extractions have essentials which are necessary and on which success depends. I call them fundamentals. The first of these is sufficient anesthesia.

Those who began performing cataract extractions at the time of the advent of the instillation of cocaine hydrochloride may still find the drug sufficient, but later generations have added subconjunctival injections, various restraining contraptions and speculums, pseudomesmerism and personality and finally the Van Lint akinesia, retrobulbar injection, nerve block and combination muscle and lid stitches. I advise these measures. After many years of using instillations of cocaine hydrochloride and subconjunctival injections, the time has come for faultless anesthesia. I have marveled at patients' fortitude and good behavior, but there have always been the uncertainties; patients are generally under a strain, and operators are on the qui vive. Every surgeon has had serious times. Why deny them? To have the perfect operation ruined by a move, a twitch or a touch is heartbreaking. A patient cannot wink if the eyelids are held by stitches. If an operator has an opinion concerning an operative technic, he should enjoy it but he should not make the patient pay for it.

At this stage, one needs: one or two hypodermic syringes; a long needle, a retrobulbar needle and a short needle; fixation forceps for the conjunctiva (fine, single toothed), and fine, strong and smooth black thread.

The important thing about the hypodermic syringe is the needle. For subconjunctival injection, a short sharp needle is used which punctures easily and escapes vessels; for producing the Van Lint akinesia, the 3 to 3.5 cm. thin needle passes through lax tissues with the least push. All should be lock needles. If one uses procaine hydrochloride, and it is preferable for deep injection, a 4 per cent solution with or without epinephrine is best. Akinesia may be unnecessary, but it is never contraindicated, and it eliminates the lid suture and abolishes the dangerous wink. A suture through the superior rectus muscle is a safeguard. A 4 per cent solution of cocaine hydrochloride seems surest for instillation; it has never given disappointing results, and I cannot credit it with the often mentioned ills. Retrobulbar injection and nerve block may seem extreme measures, but they are valuable in intracapsular extraction, retrobulbar injection particularly.

In conclusion, I suggest revision of the prevalent fear of the general anesthetic or the exclusion of its use. The old stories of vomiting and violent postanesthesial recovery no longer hold. With experienced and

reasonably measured dosage, avertin with amylene hydrate, evipal sodium and vinethene are miracle workers. How much simpler, surer and swifter cataract extraction is under these agents, only those who have used them can believe, and to reserve them for the badly behaved or dread stricken patient is like saving one's pearls for the swine. Of anesthetics, it may be said that the importance of wise selection and practiced administration stands at least equal with the value of the agent chosen.[9a]

The practice of douching the eye with everything from a solution of mercury bichloride to physiologic solution of sodium chloride has taught me to use nothing stronger than the weakest solution. I use mercury bichloride in a concentration of 1:3,000 and sterile salt solution, but sterile water is as good. Douching the eyes is like scrubbing skin, not to be recommended.

Some operators shave the brow and cut all the lashes; some use iodine after soap and water. One should use one's own method of preparation, but with a purpose. Some operators cover every inch of the face and work in a cotton bound hole. I suggest the simplest regimen and a brave consistency. Much modern "sterilization" is humorous.

The second fundamental consists of the setup.

One should become acquainted with the tools of the trade. With large illustrated catalogues at hand, one may be confused by the multitude of apparently necessary instruments. It is well to remember that the prime instrument, a good hand, dictates the setup, but since every attack on continuity opens possibilities of disaster, one should be wisely armed.

Good tools are built on mechanical principles, and good mechanics should know their uses, their handling and their limitations. Tools are right and left handed. They have puncturing and cutting points. They grip by pressure or by teeth. Blades are flat and hollow ground with variously shaped heels, bellies and points. Scissors are the triumph of the cutlerer. They are normally right handed but come left handed, pointed, blunt or curved. Mechanics spend hours selecting and conditioning their tools, while some surgeons order theirs by mail and take a nurse's word for their conditioning; yet mechanics deal with material, surgeons with life.

The instruments are considered in order of use.

"Ten thousand speculums and not a good one" is a common complaint. The human face is not symmetric; however, from a stock of several spring and lock speculums, a satisfactory and easily removable instrument is selected. I like the Smith speculum because it is not too stiff and is of proper size; it has fenestrated or solid wings. It takes

9a. Hewer, G. L.: Recent Advances in Anaesthesia and Analgesia, Philadelphia, P. Blakiston's Son & Co., 1937. Spaeth, E. B.: Principles and Practice of Ophthalmic Surgery, Philadelphia, Lea & Febiger, 1939, chap. 1.

time to remove lock speculums. Malleable wings are procurable. With a trained assistant, hooks are excellent. The best type is the simplest one that does not distort the commissure.

Fixation forceps should be substantial and one, two or three toothed, mouse or rat; they should be easy to hold and large enough to handle securely when compressing and releasing them and should have strong, cleanly cut jaws that meet accurately. There are double and angle jawed. However, holding an intractable eye is a dangerous procedure. Elschnig's forceps has a deep grip.

The knife and scissors are the surgeon's sun and shield. They should be perfect. It is difficult to thrust a dull or barbed point through the sclera or cornea, and a needle point is no proof of a keen blade. (One should learn to use a small stone.) A hand-forged Graefe knife of the right length, width and thickness and with a good handle will obey one's hand. The Smith knife has a javeline point and a straight cutting blade and is fascinatingly swift. All cutting instruments are saws, sharp or dull. To cut with them, a sawing motion is required; pushing simply impedes their progress. "Let the knife work," said Henry Smith. Use a "forward and back a full sweep," said Herman Knapp. In advancing and withdrawing a knife, the edge is kept against the cut, toe on advance, heel on withdraw. With practice, one learns to use the full length of edge and may easily finish the section with the onward sweep, but this is unwise if a conjunctival flap is wanted. Irregular sections are caused by failure to keep the knife snugly against its kerf.

Scissors are normally right handed and are difficult to select and troublesome to maintain. According to Knapp,[10] needle points are dangerous for work on the eye and should be abolished. One should try the scissors on one's face, and if they scratch, a stone should be used; the blades should make continuous contact as they close. The rings should accommodate the fingers, and the instrument should be strong enough to cut the tissue cleanly; a squeezing scissors is an abomination. An iris scissors of the de Wecker pince-ciseaux sort is short and permits the using hand to rest on the patient's head.

In iris and capsule forceps, perfection of jaws and finish must be had. Each pattern has its champion, but given delicacy and understanding hands any one will serve, the simpler being the better. H. Knapp's, de Wecker's and Smith's forceps fill all requirements: Toothed jaws are not indispensable. Kalt's original capsule forceps cannot be excelled.

The iris repositor should have one end olive shaped or probe pointed and the other end flattened and grooved; both should be malleable. It is well to have two repositors, as they are so easily fouled. The double-ended instrument is not objectionable and is often a time saver.

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10. Knapp, cited by Beard.[11]

Cystitomes vary, but one should be able to see their cutting point through the cornea. I was trained to use the Knapp instrument. The tiny bistoury is attractive.

The Henry Smith intracapsular instruments are indispensable, and I oppose their modification; made of German silver, they can be used when it is necessary to employ a magnet. Other than the large strabismus hook, Fisher's lid hook (a malleable modification of Desmarres' instrument) is useful. Green's right and left speculums fill certain needs, but one will escape having to use a retractor if one perfects one's anesthesia.

The loop, Agnew hook and spatula and needle (Fisher) have their places. The small asepto syringe with malleable anterior chamber tip does away with the old methods of irrigation and apparatus.

For recovering the capsule or its remains, a tissue forceps is best; its bite should not be too small, for often a gentle, patient teasing is necessary, and too narrow a bite may tear out.

All instruments should be strong, clean, and sharp after sterilization as well as before.

The best list of ophthalmic instruments, with illustrations and instructions, appears in Beard's "Ophthalmic Surgery," [11] a master book. Elliot's "Care of Eye Cases" [12] is an individual and delightful handbook.

The third fundamental of cataract extraction is technic.

After one is convinced of one's ability to perform the selected type of extraction, the setup should be inspected before, not as one begins, the operation. If one prefers instruments in a certain order, one should have them so. If the operator wears glasses, they should be cleaned. If his temper is bad, he should not operate. The patient should never be scolded, and the operator should never raise his voice or show surprise or tension by word, move or sigh. Patients are listeners, and although their interpretation of remarks made in the operating room may be comical, it may also be unfortunate. Tomblike silence is oppressive, but facetiousness is unwise.

The questions of what to wear, how to wash up, the time of day to operate, the color schemes of the operating room and whether to operate on a bed, table or chair are individual and environmental matters. I have done some of my best and worst work under all conditions. A rocking chair with books to keep it still, a deal table, a dingy kitchen back of a saloon, a tent on the Sahara and a perfectly equipped operating room are all in the day's work. Cleanliness and sufficient light are

11. Beard, C. H.: Ophthalmic Surgery, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1914.

12. Elliot, R. H.: Care of Eye Cases, New York, Oxford University Press, 1921.

necessary, and since the operation is never an emergency measure, one should wait until these can be obtained.

An airy room, not too large and of agreeable temperature, a comfortable posture and quiet are necessary for all concerned. If one has "no nerves," one may smile at a banging door, a screaming child or the fall of a pus basin on a tile floor, but such noises distract and sometimes startle some operators and patients. If one is operating on a patient in bed or on a table, one should be particular about a pillow. The operator wants a relaxed patient, and the position of the skull, neck and bust should be noted. Thin hair pillows which can be folded to various thicknesses are serviceable. One will do better, if one has a choice in the matter, to operate sitting rather than standing, and for obvious reasons. Modern hospital beds leave nothing to be desired. If the Indian or Madras bandage is used, it must be fitted to the patient and in position. Two sterile towels, clamps and measuring aperture for the face will cover all that needs be covered. I prefer seeing my patient's face.

One should begin operating on time. A sure hold is taken of the eyeball at 7, 6 or 5 o'clock, close to the cornea and engaging the episcleral tissue. The holding hand is supported on the face without pressure; the eyeball can be moved if one wishes, but one should never press, for pressure will cause the iris to override the advancing knife. While iridectomy and capsulotomy may be purposely performed with the section, it is bad when they are done accidentally.

A wide section is made from angle to angle, sides and top, with a liberal conjunctival flap. Let others argue if they will, but the section should be wide. Plums, grapes and pig's and cat's eyes may be used for making practice sections. They should be as symmetric and smooth as possible and made with the best hand. They must be wide, as a section the width of half a cornea is often too small. The frequent postoperative talk about "stubborn lenses," "lens molding," "stiff irides" and "tender capsules" is thus avoided.

Operators have long been told how to increase the size of the scant section with scissors. This is not difficult with a straight, strong, smooth-pointed scissors and is far better done before than after a trial at expression. In fact, when the extremely shallow anterior chamber makes the midcorneal section impossible without wounding the iris, the wise operator takes the shorter chord and at once enlarges the section with scissors. It is well to practice cutting of cornea and to recognize its need quickly, for on its omission hangs the doom of many an extraction.

Decision must be made as to whether or not to perform an iridectomy. If one is a slave to rules, it is best to make a large disfiguring keyhole, but it is better to study the iris, to dilate it and learn its habits.

There are soft flabby irides, stiff inflexible irides and irides that bleed at a touch. I advise the surgeon to respect them. If a peripheral buttonhole is desired, a Kalt hook or a tiny-tipped nontoothed forceps is used, and excision is made with small de Wecker scissors; the scissors should not be allowed to catch the hook or forceps. The consensus is that an iridectomy of some sort prevents prolapse of the iris; my teachers are of that opinion, but I cannot agree with them. I have used atropine, physostigmine salicylate and bandages; and I have used every sort of iridectomy, and again I have omitted all these measures. I believe that prolapses are due to tension and poor irides and are erratic as to site and time of occurrence. A good dose of codeine or barbital before and after operation seems equally efficient. Pathologic irides should be iridectomized to expedite delivery of the lens. It should be with the eye, as elsewhere, the less the trauma the milder the reaction. Naturally a keyhole iridectomy gives more room in an unclean chamber.

A résumé of studies and investigation as to the cause of prolapse of the iris seems at times fruitful; preventives based on such studies are provocative of hope, but thus far their continued use disappoints. (A personal experience runs something like this.) In eight extractions, a double peripheral buttonhole and two corneal stitches gave 100 per cent successful results. In the following 5 cases, simple extraction, 4 of them intracapsular, gave 100 per cent successful results. In the next 14 operations there were 7 prolapses and 2 incarcerations. No doubt a careful study of the ocular condition and history will explain and perhaps foretell prolapse; perhaps a continuous record of a patient's behavior and his ocular tension after operation will elicit causes. The conduct of the iris in other operations seems likewise unamenable to rule. Finally, the statistical reports of equally dependable operators with their favorite methods do not improve results or win general acceptance.

With regard to the toilet, one should not leave much debris or blood; both are foreign bodies, and their absorption is uncertain. Whatever method the operator uses, it should be carried out painstakingly. Fear and haste in operation are envoys of failure. The anterior chamber can be cleansed by irrigation. It is easy and safe, and an excellent repositor of iris, entire or cut. The advantage of intracapsular extraction lies in the fact that it has no aftermath, rarely even iritis or glaucoma.

If the intracapsular operation is performed, and it should be, the following facts may be noted: 1. Conjunctival flaps are not obstacles; neither is a healthy uncut iris. Both are safeguards. 2. The weakest moment in the intracapsular operation is during reposition of the iris, and it is here that full anesthesia and the muscle or lid stitch simplify the procedure. 3. The tragedies of the intracapsular technic are the small section and poor anesthesia; after these major errors come prolapse

of the vitreous and iris, reversion of the cornea, high astigmatism and even worse complications.

In every type of operation for cataract the lens must pass through the opening provided either in its entirety or piecemeal. Is the lens free to move? Is the passage large enough? On the answer depends the beauty, ease and completeness of extraction. One must liberate the lens or its contents. One may dislocate the lens by the Smith, Kalt, Knapp or Barraquer technic, and yet it will not pass safely through a small opening; its contents may be liberated by means of forceps, tome or error, and an eye blind with debris will result.

Henry Smith was the first to use definitely direct external pressure to dislocate the lens; with other methods, the eyeball is entered. Whatsoever enters a full sphere must displace the contents. Whatever the method of choice, a correctly measured external pressure alone safely expresses the lens or its remains. I know of no teaching description of lens expression to equal that of its master.[13] The most conspicuous errors made in the dislocation of the lens are, first, the institution of pressure on the lens instead of below it, and, second, failure to pull the cornea toward the patient's feet. In fact, here as elsewhere one's technic must be purposeful and accurate. In extracapsular expression, the pressure is toward the optic nerve.

After one has completed a successful extraction, the speculum must be removed. I have seen this final maneuver bring disaster; the lid stitch is valuable here, because it absolutely prevents such an occurrence. It is a good rule to cultivate the habit of engaging and releasing the upper wing of the speculum first.

What medications should be used before bandaging the eye? The answer is, What will medicine do? Atropine does little but paralyze accommodation after marginal iridectomy. If it causes dilatation after peripheral iridectomy, it occludes the buttonholes, and a wrinkled iris results. Physostigmine salicylate should have the opposite effect. With the anterior chamber full of detritus, atropine should be employed. When iridectomy has not been done, both drugs act tardily but normally. Without definite indication, why use medicine? A little ointment, yellow mercuric oxide, mercury bichloride or boric acid in petrolatum, applied along the closed edges of the lids is reasonable. Nothing kills faith in medicine like its untimely or thoughtless administration.

Even with the most proficient operator, one misfortune can happen, such as prolapse of the vitreous before delivery of the lens. (I overstep the bounds of this paper in giving the care of the vitreous.) A Smith spatula is slipped through the presenting vitreous, down behind the lens; with the Smith hook, its tip on the cornea below the edge of the

13. Smith, H.: The Treatment of Cataract and Some Other Common Ocular Affections, ed. 2, London, Butterworth & Company, 1928, p. 99.

lens, gentle upwardbearing pressure is exerted, and the lens will proceed up the spatula. It is frightsome, but it is expeditious and safe. One should not use sharp hooks unless acquainted with their vagaries.

The fourth fundamental of cataract extraction pertains to the bandage.

The best bandage is that which is most comfortable and easiest to maintain. The perfect splint for an eye is the eyelid, which will remain closed and still if evenly supported. One should not judge a bandage by its outward appearance; beneath, bandages may be uneven, too light, too loose or too hot. The Indian, or six-tailed bandage, the Madras bandage and the Moorfield bandage are good, but a layer of wet absorbant cotton, molded to the closed eyelid and held by an elliptically-shaped patch, should underlie every bandage or shield. Body movements are not transferred to the eye. I have known patients to travel miles safely after operation. One should always make the first dressing oneself; it is unfair to leave it to others. Bandages are for protection, support or pressure, not for culture chambers. They should not be made like the jacket of a popular novel—mostly color, gloss and misrepresentation. One should finish as well as begin bandaging cleanly.

Cataract extraction is an operation for the art museum, artistic, skilful and dramatic. Those who work with such canvas, color and brush should have the physician's art, the scholar's mind and the magician's hands. To teach cataract extraction, one reviews one's own struggles. Sporadic seances with pig or kitten eyes do not advance one's skill any more than irregular and undisciplined flings in other subjects. To evert an eyelid is not enough; it must be done quickly and usefully, with swollen, lashless, tender, diseased lids, in the infant, the old, the timid and the difficult. To insert or remove a speculum as I have seen it done in high places is barbarous. Scratched corneas are dangerous. To what greater extent must the section be a triumph of artistic accuracy?

One must attain this celerity, this effortless speed, by continued practice, as one would the cadenza on the piano or the pirouette of the ballet or as one would do the curves and surfacing in carving or chiseling. One must abhor mediocrity! Only daily practice suffices to train the hand. The difficulties of extraction are not greater than those of other operations, but the faulty section cannot be altered, and the scar, though good to look at, is a scar that sight cannot penetrate.

It has been said that operating on a hundred kitten eyes will banish hesitancy. Faith should not be put in numbers. One hundred trials showing similar error or imperfection teach nothing. To have hands like a Knapp or a Smith, one must work and think like a Knapp or a Smith. Kalt said that he made ten thousand stitches before he published the description of his corneal stitch, but it was the painstaking concentration rather than number of trials that gave the final results.

Perfection has not been achieved by men of any one nation, but a definite regularity and accuracy are found among the the English, French and German surgeons; for stereotyped work, amazing in its machine-like precision, one has only to watch those of first rank in foreign hospitals. Characterized by heartlessness in Germany, egotism in Austria, spontaneity in France and classicism in England, these surgeons' offerings should not be spurned over here, where the people are a composite of all. The stars are of no people, nation or time but shine forth from pole to pole. Some persons excel in ability to escape their just deserts, and it is an art to bring victory out of defeat, but for the aspiring generation the higher art is not to countenance defeat. I quote the following lines from Beard: "After all, it is here just as with surgery in general, that subtle something known as 'personal equation' is a tremendous factor." To this truth, I add, "to be valued but never depended upon."

The fifth fundamental of cataract extraction is hospitalization.

The remark of Herman Knapp that "many can do a good extraction, but it takes a good man to discharge a seeing eye" is more and more confirmed with the years. Too many operators seem to lose interest after having fastened the bandage and trust the finale to interns, nurses and nature. Of the three, nature is probably the best ally. However such lack of interest should not be. Details of routine and particularized care are found in many books, but the important thing is that the surgeon honor his method. Simple, sensible orders have a chance of fulfilment. Men and women of the hospital personnel are no different from the surgeon. The impossible or fantastic are invitations to neglect.

I shall consider a few factors which make for the success of an operation.

1. Immobilization of the patient is impossible in hot weather; it is also impossible if the patient is aged or senile or is stout or mentally affected. Such a measure is ridiculous and should not be attempted.

2. As to immobility of the operated eye and its fellow, if a properly fitting, light-occluding bandage is applied, the eyes will remain quiet. Movements of the skull do not affect it.

3 It is often more disturbing for the patient to use a bed pan than a commode, and it is easier for most persons to evacuate in a sitting position.

4. Patients move themselves with less effort and disturbance than does the kindly-intentioned pulling, lugging and shoving by an attendant, often too weak physically to handle the patient's weight.

5. Leading the blind by placing the blind person's hands on a guide's shoulders and proceeding slowly never disturbs the eyes. Patients are quieter when they are wisely directed than restrained.

6. In regard to bandages, the first cover should always be secured with adhesive tape. If the bandage loosens before one wishes to remove the molded splint, one can renew the tape. Some operators examine the eye in twenty-four hours and others later. The time of examination should be a matter of choice and not of habit. I have found that, barring accidents, the eye that needs inspection within twenty-four, forty-eight or even sixty hours makes its need evident to nurse, companion or doctor. Symptoms or signs should be guides, and the practiced surgeon seldom misses them.

What can be done at an early examination? Aside from replacing a reverted cornea (and this happens at the operation), one can only apply another bandage.

What may happen at early inspection? The wound, in part or in its entirety, may reopen, or a prolapse of the iris or infection may occur. The surgeon should measure these facts and act accordingly.

When changing the bandage, one should not fail to examine it and the eye. A dressing tray should be nearby ready for an emergency.

7. Because these patients are not sick, they often suffer neglect. They have wandered and fallen through doors, elevators and windows; their eyes have been injured through perfectly placed bandages by a false step or by contusion by the doctor, the nurse or themselves, and they have remained silent. Patients with cataract should be regularly visited; their bedside charts should be regularly filled, and the operator should have them called to his attention in case he forgets.

It should be remembered that when the seeing eye is uncovered these patients may run into obstacles on the blind side. They must be watched. I have lost one eye because the patient bent over and hit it on a chair back. A confrere had a patient lose both his eyes because of injury from a chair knob. One such accident suffices.

Strong light is forbidden; better, it should be prevented, but for the eye, not for the body. Sunlight, fresh air and a normal existence are essential for convalescence.

I teach my nurses to assume an interest in these patients if they do not have it. For a healthy seeing person to spend two weeks or over more or less bandaged is for him to lead an abnormal and a lonely existence. Well persons are the nuisances of the ward and the pest of the private room. The surgeon should act accordingly. Nursing of such patients is a high art. Many an eye owes its darkness to a poor physician, an uninterested nurse or a badly trained ego.

8. When shall the patient be discharged? In making a decision, the surgeon should always consider the patient's habitat and his ability to return for examination. It is difficult for a half blind person to put medicine in his own eye. In case of an accident, will the surgeon be on

hand? Every surgeon has the right to refuse to operate, but having operated he may not walk out, forget his patient or transfer his responsibility. Orders for the discharged patient may be written, printed or spoken, but they must be understood. It is a common practice for patients to be discharged from the hospital by persons other than the operator. This is quite wrong.

CRITICISMS

Having observed, operated and taught for fifty years and having always kept an open operating room with a looking glass as part of its furniture, I believe that my criticism should be helpful, as it is without malice.

I have watched operations closely in Amritzer, Berlin, Birmingham, Bombay, Boston, Cairo, Calcutta, Chicago, Edinburgh, Heidelberg, Kioto, Leipzig, Leningrad, London, Madras, Milan, Montreal, Munich, Naples, New York, Paris, Philadelphia, Rangoon, San Francisco, Strasburg, Tokio, Utrecht and Vienna, and with but one prayer, to maintain a humble and a receptive mind.

I have seen uneasy operators with poor vision and heavy "iron" clumsy hands; frequent and useless handling of instruments; irritability toward nurses and assistants; surgeons who are unacquainted with the patient; surgeons who are dependent on memory and other's "say so"; incomplete or badly arranged "setup," and delays due to change of the modus operandi. None of these conditions are excusable; even in view of all the inadvertencies of hospital management, they are "bad habits." In the same centers I have enjoyed order, peace and comfort; happy surgeons, attendants and patients; promptness, politeness and wonderful skill.

All surgeons see and commit many slips in the single operation, but a day or week of association will not fail to mark the teacher. There is a great gulf fixed between errors of mischance and those of misuse, but in either case criticism is puerile if it fails to improve the critic's practice. Some of these errors and reasons for failure are described.

1. A superficial hold may be had on the globe due to poor forceps, attenuated conjunctiva or failure to include the episcleral tissue. A dull knife point or a badly directed puncture with the knife blade held parallel with the cornea requires great pressure and tears the conjunctiva; advancing it makes a leaking wound and moves the globe. Recovery from this complex often demands a fresh grasp.

2. The knife point may stick or scratch the nose because of a deepset eye, a high nose bridge or too long a blade. This may occur if the patient's facial topography is not studied; if the selection of a shorter knife or stroke is forgotten, or if the patient jumps.

3. Unconscious pressure may be exerted with fixation forceps (a frequent and sad occurrence).

4. I have seen misfortune visit operators as they looked up to select the next instrument. One should appreciate how instantaneously head and eye can move and how swiftly time flies during interruptions. While operating, the surgeon's eye should make neither mental nor optical excursions.

5. It is alarming to see an assistant administer a drop, cold or from a height. One should avoid untrained or uninterested assistants. It is wiser to work alone. Many sad exhibitions have been due to strange environment, unsympathetic atmosphere and poor teamwork.

6. I have seen accidents occur due to poor light. Light is important, its quantity as well as its quality; it should be mellow and located so as to prevent reflexes. There are many good simple sources; but whatever the source, candle, oil, gas mantle or electricity, one should be sure that it is in working order. If circumstances compel one to have some one hold the light, one should beware of a fainting or a too interested volunteer whose slightest movement leaves the field black—a terrible dilemma. A clear northern light at sun-up is ideal. It is well, I find, not to accustom oneself to too much light.

7. An operator who has much trouble with light would do well to wear a + 1 to 2 D. sphere; it would lighten the field and, being just short of magnification, will be helpful. There are a lot of persons with vision of 20/20 who are slow sighted.

8. I have seen excellent work done by operators with tremulous hands, of which I know two sorts: One has hands that tremble only at times, like an interrupted current, and are practically still, while the other has hands which tremble erratically and uncontrollably. The latter type should not attempt extraction. I have seen it done with pitiable results.

9. I have found many ophthalmic operating rooms deficient in the simple business-like procedures of the general surgical room. There is commonly a restraint and an accumulation of self consciousness which broadcasts, "an occasion." Where reputation weighs heavily, sloppy work is common, and the attempt at clinical congresses to operate only on the eye which is considered "safe and sure" often shows a master at his worst. One may learn more when the classic operation, overturned by complications, compels resourcefulness.

A résumé of fifty years of clinical experience in cataract extraction has taught me the difficulties, the dangers, the accidents and the inspiration that surround the practice. I charge no one with less sincerity, less prayerful interest and sympathy than I hope I possess. The terrors of failure, the strain of responsibility and the burden of inefficiency and

carelessness have not passed my open door. The star performers, the commercialist and the "loud speaker," men who carp, criticize and then copy, are always with one, but for those who, like myself, carry the load, I wish to summarize the sources of most errors and failures in cataract extraction: (1) lack of a workable diagnosis, (2) insufficient anesthesia, (3) poor sight and facility, (4) poor or badly selected tools and light, (5) the wrong method, (6) poor bandage and after-care and (7) insufficient practice.

It has not been my intention to dictate or advise the type or method of extraction. Students will find that most operators endorse procedures with which they. are most successful. Résumés attempting to present unbiased views leave one widely informed but unpersuaded. The evolution of the surgeon begins with his first teacher and develops on that inspiration. Properly launched, he approaches innovations with either distrust or abandon, but his maturity will generally bear the hallmark of his origin. To support one's choice of ways and means one can easily collocate names and figures, but results will be the product of one's own hands. I have been warmed with the desire to choose words that may guide the operator step by step, disarm doubt or perplexity, intensify minutii into essentials and aid him in preparing his patient for the perfect attack.

"If ye know these things, happy are ye if ye do them."

I wish to add a golden epilogue:

One should meet errors with a brave postponement, irrespective of audience or pride.

Prolapse of the iris is best met by courageous excision, cauterization of the wound and conjunctival flap.

Prolapse of the vitreous in volume demands hopeful nursing, until infection or phthisis bulbi demands intervention.

For infection, an open eye, light, air, protein and continuous effort build reasonable defense.

Expulsive hemorrhage is no man's fault, and the best finale is delayed enucleation or a like operation. One should not bank on statistics (1 in 700). One may draw the one.

The shock of announcing an operative failure should be avoided. Time is the kindest informer and usually the most correct.

Nurses, interns, orderlies and relatives are among the factors which contribute to the accidents and complications of cataract extraction. As such, they require control.

Before operation, the surgeon is an adviser; after operation, a friend; during operation, a god.

I witnessed extractions by Herman Knapp in 1888 and by Nettleship in 1889. I have never seen either surpassed in method, skill or results.

TUBERCLE WITHIN CENTRAL RETINAL VEIN

HEMORRHAGIC GLAUCOMA; PERIPHLEBITIS RETINALIS IN OTHER EYE

F. H. VERHOEFF, M.D.
BOSTON
AND
G. VICTOR SIMPSON, M.D.
WASHINGTON, D. C.

The following case, so far as we can ascertain, is only the second in which on microscopic examination a tubercle was found in the lumen of the central vein and the first in which such a tubercle has been associated with periphlebitis retinalis in the other eye. The clinical investigation of this case was made under the supervision of one of us (G. V. S.).

REPORT OF A CASE

Cutaneous tests to 0.001 and 0.01 mg. of old tuberculin were negative; a test
A white man aged 31, a taxicab driver, was first seen in the outpatient department of the Episcopal Eye and Ear Hospital on Nov. 12, 1931, with the complaint of poor vision in the right eye for a few weeks.

A history was obtained of recurrent attacks of poor vision, followed by intervals of improvement, during the past six years. The attack which brought the patient to the hospital began a few days previously, and as in all former attacks the loss of vision had been rapid and without pain.

The vision in the right eye was reduced to perception of light with good projection. Externally the eye was normal. The pupil dilated well. With the ophthalmoscope, a fundus reflex could be obtained only at the periphery, and here it was faint. Slit lamp examination showed a normal cornea and iris but some changes in the posterior part of the lens. It was evident that a severe hemorrhage had taken place into the vitreous.

Vision in the left eye was 20/15, and the eye was normal in every respect. No hemorrhages were seen in any part of the retina.
to 0.1 mg. was moderately positive. The exact size of the reaction was not stated on the record. Clinical and roentgen study of the chest gave negative results. Roentgen examination of the sinuses showed hyperplasia and exudate in the left antrum and a polyp in the right antrum, which was not verified by the injection of poppyseed oil. No treatment of the sinuses was undertaken. The

Wassermann reaction of the blood was negative on three examinations. Examination of the urine showed an occasional hyaline cast. The red blood cell count was 5,180,000. The white cell count varied from 7,000 to 11,000. The blood smear showed nothing striking.

A diagnosis was made of tuberculous phlebitis with recurrent hemorrhages in the vitreous of the right eye. Subcutaneous injections of tuberculin in graduated doses were given from November 1931 to August 1932.

The vitreous of the right eye gradually cleared, and the vision returned to 20/100. Examination of the fundus of the right eye in April 1934 revealed some opacities of the vitreous, a normal optic disk and a good deal of scar tissue over the entire lower portion of the retina, spreading upward into the macular area and forward into the vitreous. The left eye was normal.

In July 1933 the patient was admitted to the Georgetown Hospital for surgical treatment of inguinal adenitis. According to the pathologic report, the gland removed was a solid lymph gland about the size of a walnut. There was no gross suppuration. Sections showed complete disappearance of the germinal centers. There was diffuse fibrosis and invasion by large endothelial-like cells; an occasional multinucleated cell was seen but no large cells or eosinophils. The condition seemed to be typical lymphogranulomatosis or Hodgkin's disease. Sections of this gland were submitted to two general pathologists of wide experience. They did not concur in the diagnosis of Hodgkin's disease, however, but regarded the condition much more likely to be chronic inflammatory hyperplasia.

On May 14, 1934 the patient visited the clinic complaining of sudden loss of vision in the left eye twenty-four hours previously. The vision was reduced to poor perception of light, and examination showed that complete closure of the central vein had occurred. The branches of the vein were enormously dilated, and there were numerous hemorrhages throughout the entire retina. Three days later the patient returned with an acute rise in tension in the left eye, accompanied by a great deal of pain. The patient was hospitalized, and medical treatment from May 17 to May 28 failed to give any relief. On May 28 a broad iridectomy was performed, at which time a moderate hemorrhage into the anterior chamber occurred, and the next day the anterior chamber was filled with blood. The patient obtained no relief from the pain, and the left eye was enucleated on June 14.

At this time the condition of the right eye was unchanged. The central vision was 20/100, and there was a fair field.

In December 1939, when the patient was last seen, five years after the left eye was removed, the condition of the right eye remained about the same. An artery in the upper temporal fundus was found occluded. The visual acuity was still 20/100. The patient was in excellent health, had increased considerably in weight and had had no occasion to consult his family physician during this time. There had been no recurrence of the inguinal adenitis.

Pathologic Examination (F. H. V.).—Macroscopic Examination: The enucleated eye had been in a 4 per cent dilution of formaldehyde for three days when received. It was then placed in a solution of 70 per cent alcohol containing 2.5 per cent hydrochloric acid and after twenty-four hours was opened by horizontal section in the usual manner. The anterior chamber was found to be full of blood; the vitreous was slightly turbid. The retina, in situ, showed numerous hemorrhages, and there was a slight amount of blood extending from the disk into the vitreous. The eye was embedded in pyroxylin and sectioned horizontally until the sections

included the upper margin of the optic disk. Numerous sections were stained in hematoxylin and eosin. Serial cross sections were made of the remaining optic nerve and disk, including the central retinal vessels.

Microscopic Examination: The corneal epithelium was normal. The nuclei of the corneal corpuscles in the deepest layers of the cornea progressively disappeared from near the periphery to the center of the cornea, where they were entirely invisible in the posterior half of the stroma. The endothelium was absent in short stretches. On each side there was peripheral anterior synechia of about 1 mm., which on the nasal side in some sections had been freed by hemorrhage. The iris, thin and fibrotic, showed ectropion uveae and was coated with a vascularized membrane, which was disorganized and in places enormously distended by hemorrhage and continued into a thin pupillary membrane. The hemorrhage had broken into and distended the anterior chamber with blood. The sections did not pass through the site of the iridectomy. The lens was normal. The ciliary body was compressed and its processes congested. On its surface there was a moderate amount of blood, within which were many macrophages filled with red blood corpuscles. The choroid was normal. The iris, choroid, sclera and retina were free from infiltration with chronic inflammatory cells. The retina showed numerous hemorrhagic extravasates as far forward as the equator. It was everywhere free from evident edema. It showed no tubercles. The macula was distorted, and beneath it was a hemorrhagic extravasate about as thick as the retina. There was also a small hemorrhagic extravasate in front of the macula. Over the surface of the disk and extending also over the retina to the fovea was a vascularized membrane. The distortion of the macula was no doubt due partly to this membrane and partly to hemorrhage. From the nasal margin of this membrane on the disk a delicate strand of tissue extended for a considerable distance into the vitreous (retinitis proliferans). In the macula there was some hematogenous pigment. Ganglion cells remained abundant in the macula but were greatly reduced in number elsewhere. The retinal vessels showed conspicuous changes only in the vicinity of the disk and macula. Here there were numerous actively proliferating small vessels from which the vessels in the vascularized membrane were obviously derived. Some of the arteries near the macula showed marked subendothelial proliferation, and one large artery here was completely occluded by such proliferation. The choroidal vessels and the posterior ciliary vessels seen in the sections were free from endovasculitis. Only a small part of the periphery of the disk was included in the last horizontal sections. These showed the lamina cribrosa curved deeply backward but did not expose the glaucomatous cup.

Serial cross sections of the remaining portion of the optic nerve and disk showed a glaucomatous cup partly filled with connective tissue rich in newly formed capillaries and vessels. The central artery was in all sections patent and free from endarteritis. As the serial sections were examined from behind forward, the central vein was first found to be patent and free from endophlebitis, but about 1 mm. behind the lamina cribrosa both central vessels, but especially the vein, were surrounded by many lymphocytes. Projecting into the lumen of the vein from one side there appeared a mass of cells, which, within the range of a few sections, became so large as almost completely to occlude the lumen (fig. 1). At the same time the lymphocytic infiltration rapidly became less and practically disappeared before the lamina cribrosa was reached. The cells within the lumen had the appearance of epithelioid cells such as are seen in tubercles. No typical Langhans' giant cells were found, but there were many multinucleated cells. Just

within the lamina cribrosa the lumen of the vein was completely occluded. Here the cells showed more cytoplasm, and fibrosis was evidently taking place. Farther forward the site of the vein appeared as an irregular area of fibrous tissue which was being pervaded by neuroglia and which finally merged with connective tissue at the bottom of the glaucomatous cup. The lumen of the vein never again became recognizable, but within the disk three relatively large distended veins appeared which were evidently main branches of the central vein. Farther forward, vessels became more numerous, until finally the vascularized membrane on the surface of the disk came into view. Just in front of the lamina cribrosa there was a nodular collection of lymphocytes around the site of the central vessels.

In several longitudinal sections one large venous collateral was seen emerging from the lamina cribrosa and coursing backward in the pial sheath.
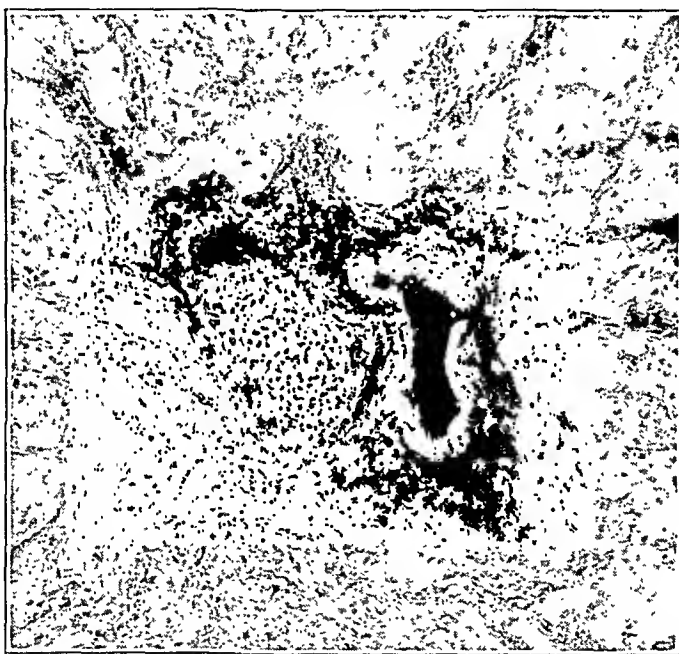
Fig. 1.—Tubercle within the central retinal vein. Here the tubercle does not completely obstruct the lumen. Hematoxylin and eosin; × 140.

In addition to the tubercle within the central vein, five tubercles of miliary size were found in relation with the optic nerve. Two of these were in the pia, one (fig. 2) in the sections just behind the obstruction in the vein and the second in sections passing through the obstruction. The third tubercle, the smallest, was within the arachnoid in these same sections (fig. 3). The fourth was at the end of the subvaginal space. The fifth was in the episcleral tissue 1.8 mm. outside the subvaginal space. All of these tubercles contained definite Langhans giant cells and were free from necrosis. The tubercle in the arachnoid had a mantle of lymphocytes, but the others showed almost no lymphocytic reaction around them. The largest was the episcleral tubercle. This was situated beside a vein about the size of a normal central retinal vein. Although this tubercle involved the entire thickness of the wall of the vein to the endothelium, there was no proliferation within the lumen. Close to this vein was a posterior ciliary artery and a large posterior ciliary nerve.

Fig. 2.—Tubercle in the pial sheath of the optic nerve. One giant cell is easily seen. Hematoxylin and eosin; × 80.
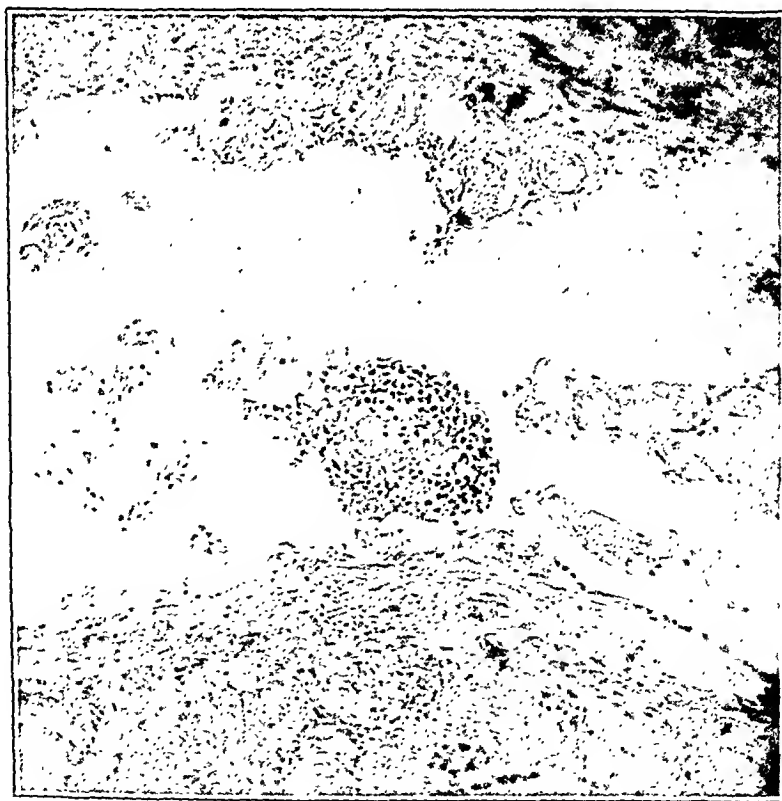
Fig. 3.—Tubercle within the arachnoid of the vaginal space around the optic nerve. It consists chiefly of two giant cells surrounded by lymphocytes. Hematoxylin and eosin; × 111.

No tubercles could be found elsewhere in the eye, including the retina and choroid.

Seven sections through the tubercle in the central vein were stained in carbolfuchsin differentially for tubercle bacilli. Three of these included one of the tubercles in the pia. No bacilli could be found in any of these sections.

<div align="center">COMMENT</div>

It is clearly evident in this case that, as concerns the left eye, the sequence of events was, first, obstruction of the central retinal vein within and just behind the lamina cribrosa; second, marked hemorrhagic retinitis, and finally, glaucoma which required enucleation of the eye. The changes within the eye were similar to those often seen after obstruction of the central vein from senile endophlebitis. The severity of the hemorrhagic retinitis and the formation of vascularized tissue on the surface of the disk and retina, with beginning retinitis proliferans, were no doubt due to the rapidity with which the obstruction occurred. The obstruction of a macular artery by proliferation of the intima presumably resulted from high intravascular pressure produced by the obstruction of the venous outflow. The obstruction of the central vein resulted from a nodular mass of epithelioid cells within its lumen. If tuberculous lesions can be identified by their histologic structure, then this nodule and the five small foci of epithelioid cells in the pia, arachnoid and dural sheath of the optic nerve were tubercles. It is true that they were free from caseation, that they caused almost no reaction around them and that no bacilli were found in them, but these facts obtain for most ocular lesions supposed to be tuberculous. The tubercles were similar to those that have been found in the retina in cases of periphlebitis retinalis, except that in these cases the tubercles are situated chiefly outside the walls of veins, whereas in the central vein the tubercle was within the lumen.

The fact that periphlebitis retinalis existed in the right eye in the present case tends to dissolve the doubt that this retinal condition is due to tuberculosis. It also indicates that the tubercle in the central vein of the left eye was dependent on the same general conditions that favor the occurrence of retinal tubercles. Just what these conditions are is unknown. It is evident, however, that in the present case the tubercle in the central vein was metastatic through the blood. The other tubercles were so situated that they might have resulted from bacilli carried from the tubercle in the vein along perivascular spaces of branches of the central vein. The fact that no tubercles were found elsewhere in the eye makes this possibility a strong probability. A tubercle within a vein is, of course, not an infrequent finding elsewhere in the body. The fact that only once before has it been observed in the central retinal

vein is possibly because serial sections are seldom made of the central vessels in such cases. The occurrence of the enlarged inguinal gland, which was removed in 1933, was probably purely coincidental, since such glands not infrequently occur without obvious cause and unassociated with any other recognizable pathologic condition.

The only similar case we have found in the literature was reported by Šafář in 1928.[1] In the left eye removed from a youth aged 18 he found in serial longitudinal sections a tubercle within the lumen of the central vein, just behind the lamina cribrosa. This did not quite obstruct the lumen. In the pia at the end of the subvaginal space he found another tubercle. Around a ciliary nerve and its accompanying vessels he found lymphocytic infiltration. The eye showed the typical picture of severe hemorrhagic glaucoma, with retinitis proliferans. This case was essentially identical with ours, with the notable exception that in Šafář's case the fellow eye was normal. Šafář, in addition, found a large retinal vein also obstructed by a tubercle and numerous minute retinal tubercles at the periphery of the fundus. The lymphocytic infiltration around the ciliary nerve may have been due to a tubercle farther back, such as was present in our case, but too far back to be included in the specimen. Šafář also was unable to find bacilli in the tuberculous lesions. He regarded the tubercle in the central vein and that in the pia as independent and directly metastatic from the blood. He did not consider the possibility of the pial tubercle arising secondarily from the tubercle in the central vein. In his case it seems possible that the tubercle in the central vein was secondary to the tubercle he found in a retinal vein.

A few cases have been described, notably 3 by Urbanek,[2] in which a clinical diagnosis of tuberculous partial or complete "thrombosis" of the central vein has been made. In these cases the vision of the affected eye was never completely abolished and later greatly improved, in 1 of the cases being completely restored. These cases considered in the light of Šafář's and ours indicate that a common cause of suddenly occurring extensive retinal hemorrhages in young persons is tuberculous endophlebitis of the central vein. They also indicate that in many such cases the circulation through the central vein becomes fully reestablished and vision restored. This is in marked contrast to cases of obstruction of the vein due to senile endophlebitis, in which vision of the affected eye is almost always permanently abolished.

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1. Šafář, K.: Ueber Drucksteigerung im Gefolge der juvenilen Netzhaut-Glaskörperblutungen und Verschluss der Zentralvene infolge tuberkulöser Phlebitis, nebst Bemerkungen über die Entstehungsweise der Netzhautgefässtuberkulose, Arch. f. Ophth. **119**:624, 1928.

2. Urbanek, J.: Die Bedeutung der Tuberkulose fur die entzündlichen Erkrankungen des Uvealtractus, Berlin, S. Karger, 1929.

SUMMARY AND CONCLUSIONS

A case of hemorrhagic glaucoma in a young person is described, in which microscopic examination showed a tubercle obstructing the lumen of the central retinal vein. In this case the other eye had previously been affected with periphlebitis retinalis.

This case lends strong support to the view that periphlebitis retinalis is tuberculous in nature.

This case and a similar one reported by Šafář, considered in connection with certain clinical cases reported in the literature, indicate that partial or complete tuberculous obstruction of the central vein is a frequent cause of suddenly occurring extensive retinal hemorrhages in young persons. When obstruction of the vein is so caused, more or less complete restoration of vision may occur.

ABSTRACT OF DISCUSSION

Dr. Jonas S. Friedenwald, Baltimore: I should like to report 2 cases which are in some respects related to that reported by Dr. Verhoeff and Dr. Simpson. These are cases of intraocular inflammatory disease caused by tuberculosis or a similar agent and complicated by occlusion of the central retinal vein and hemorrhagic glaucoma.

The patient in the first case is a white man of 28 who has been under the care of his physician, Dr. Tonolla, since May 1939 on account of pulmonary tuberculosis. Dr. Tonolla supplied the following data concerning the medical history. The patient complained at the onset of a morning cough, loss of weight and night sweats, and examination showed lesions in the upper lobes of both lungs with cavitation in the right lobe.

Tubercle bacilli were found in the sputum. After hospitalization of the patient and treatment with pneumothorax, he became asymptomatic and was ambulatory in September.

In October 1939 he had acute frontal sinusitis, which rapidly cleared under local treatment. Six weeks later he complained of blurred vision in the right eye. I saw him first one month after the onset of his ocular symptoms, when he showed the picture of optic neuritis with a slightly turbid vitreous, intense swelling and protrusion of the optic disk, enormous engorgement of the retinal veins, many hemorrhages and exudates and almost complete loss of vision in his right eye. His left eye was perfectly healthy. A Wassermann test and an agglutination test for Brucella gave negative results. Physical examination revealed an arrested pulmonary lesion with pneumothorax.

Two weeks later the eye became painful and congested, with a steamy cornea, a dilated pupil and a marked rise of intraocular pressure. Local medication failed to relieve the condition, and since the patient began to lose weight and was unable to sleep on account of pain, enucleation was performed two and one-half weeks after the onset of the glaucoma.

Histologic study showed the changes in the iris characteristic of hemorrhagic glaucoma. At the margin of the optic disk there was a caseous and hemorrhagic lesion.

The central retinal vein was occluded by a nontuberculous proliferation of the endothelium, but one of the peripheral retinal branches contained an endovascular tubercle. Many hemorrhages were scattered through the retina, and there were numerous newly formed vessels on the surface of the retina and in the optic disk. The optic disk showed a glaucomatous excavation. In the optic nerve behind the disk there was a nodular accumulation of mononuclear cells which resembled the tubercle in the optic nerve described by Dr. Verhoeff.

My interpretation of this case is that there was a tuberculous optic neuritis with tuberculous retinal phlebitis, retinal venous occlusion and hemorrhagic glaucoma. Unlike the case reported by Dr. Verhoeff and Dr. Simpson, the venous occlusion was not certainly due to an endovascular tubercle.

The second patient, D. R., a white man of 64, had begun to lose the vision of his right eye in 1926, and since 1930 he had had bare perception of light. In February 1940 the eye became painful and congested. Two weeks later he was admitted to the Wilmer Ophthalmological Institute and was found to show marked congestion of the right eye, with a steamy cornea and hyphema. There were a few cellular deposits on the back of the cornea, posterior synechia, cataract, bare perception of light and tension of 40 (Schiötz). The left eye was normal except for an immature senile cataract.

The right eye was removed and on histologic study revealed a tubercle in the ciliary body eroding into the vitreous. The retinal veins showed several inflammatory lesions not certainly tuberculous. The central vein was occluded by endothelial proliferation. There was a glaucomatous excavation of the optic disk and many newly formed vessels in and on the retina. In the choroid an extensive inflammatory lesion was found which consisted mainly of epithelioid cells and giant cells with a surrounding narrow zone of lymphocytes. There was necrosis of the overlying retina but no caseation. Within the choroidal lesion a small choroidal vein filled with tubercle was found. The massive epithelioid cell lesion without caseation raised the question as to whether the condition was really of tuberculous origin.

Because of these remarkable pathologic changes, the patient was sent for and readmitted to the institute in April. A careful survey for possible etiologic factors revealed no foci of infection in the nose or throat, benign prostatic hypertrophy with mild chronic prostatitis and no periapically infected teeth.

The Wassermann reaction of the blood was negative on two tests. A positive reaction was obtained to 0.1 mg. of old tuberculin but no reaction occurred to 0.01 mg. The reaction of the complement fixation test for gonococcus was doubtfully positive. There was no reaction to the Frei or the Ito test. Biopsy of an inguinal lymph node showed normal tissue. There was a strongly positive reaction to the opsonic test for Brucella abortis and Brucella suis. Agglutination tests with Br. abortis and Br. suis gave negative results, and the reaction to the complement fixation test was moderately positive. No response was elicited to cutaneous tests for Br. abortis and Br. suis.

It is impossible on the basis of these findings to decide whether the inflammatory lesion in this case was tuberculous or due to infection with Brucella.

These cases resemble that reported by Dr. Verhoeff and Dr. Simpson in that there were granulomatous intraocular inflammation with endovenous tubercles, occlusion of the central retinal vein and hemorrhagic glaucoma. It would seem possible that the syndrome to which attention has been called may not be as rare as the previous failure to describe it might indicate.

DR. ARTHUR J. BEDELL, Albany, N. Y.: Dr. Verhoeff and Dr. Simpson have drawn conclusions which indicate that partial or complete tuberculous thrombosis of the central retinal vein is a frequent cause of suddenly occurring extensive retinal hemorrhages.

I wonder if this is entirely justified from their meager data. I should like to ask them how often they have seen a frank hemorrhage of the retinal artery from its clinical onset to complete resolution after having filled much of the vitreous with blood?

To make the question pertinent, I will show a series of photographs of the fundus of a woman of 30. In the first, the blood is from an artery.

The next slide shows that the blood broke through the artery and the hemorrhage increased, filling part of the vitreous.

Later a definite proliferating band formed in the area of vascular disease.

The final photograph shows that resolution continued until the vision was completely restored and the fundus almost clear.

I should also like to ask how in the presence of marked obstruction of the central retinal vein in a young adult can the diagnosis of vascular tuberculosis be made without pathologic examination.

(Photographs illustrating 2 such cases were shown.)

In the first case gross exudate and secondary glaucoma developed in a young woman who had an evident thrombosis, and enucleation was necessary. The photographs include views of her vitreous, showing hemorrhages which came on previous to the great increase of ocular tension.

In the second case a woman of 28 presented marked perivascular changes. Hemorrhages developed but were finally absorbed by treatment. How could this condition be said to be of tuberculous origin?

The essayists have opened another path leading toward the clarification of a difficult problem.

DR. EDWARD JACKSON, Denver: This subject is one of enormous practical importance. Its practical importance, to my mind, overshadows the interesting fact in pathology that it presents, and that is that tuberculosis may exist and be concealed within the body for long periods before it is recognized.

I live in Colorado because my wife had tuberculosis. She died of tuberculosis. It was, judging from the subsequent history of the case and in looking back from the present knowledge, present for ten years before her death. She left five children, and I felt sure that they would have a better chance for life in Colorado than in the eastern United States. We went to Colorado, and they all grew up to adult life without any evidence or suggestion that they had tuberculosis.

The lesson before the members of this section is that no matter how obscure the lesion may be it may be vital for the particular patient and his family to have discovered it, even if the discovery had to be made by microscopic examination of the eye.

DR. FREDERICK H. VERHOEFF, Boston: Dr. Friedenwald's cases are interesting, and I agree with his interpretation of them. I think the fact that he could not be sure that the obstructions of the veins were tuberculous is consistent with what I found in our case. In the anterior part the obstructing mass had become so fibrotic that if I had seen only this part of the obstruction I would have been doubtful as to whether it was tuberculous. In these cases, after some time elapses the condition may change so that it cannot be recognized as tuberculous.

There is one point in regard to our case about which I am doubtful, and that is the duration of the obstruction. I have not had a chance to talk to Dr. Simpson about this, but it seems to me it is impossible for an eye to show in one month the changes that I found. According to the history, the glaucoma was only of a month's duration. If all the changes I found occurred in a month, I certainly would have to revise my ideas as to the changes hemorrhagic glaucoma can produce in an eye in this length of time.

The only one of Dr. Bedell's questions that I could understand was in regard to the frequency of tuberculous obstruction of the central retinal veins as the cause of extensive retinal hemorrhages in young persons. Our statement in regard to this did not mean that hemorrhagic retinitis is frequent in young persons but that tuberculous obstruction of the central retinal vein is a frequent cause of the condition in such cases as do occur.

I must say that it was not solely on the few cases referred to in our paper that I based my opinion. Every now and then I see a young patient with marked hemorrhagic retinitis obviously due to obstruction of the central retinal vein, and I have always been puzzled as to the cause. I should say that in the majority of them the vision is restored, sometimes completely to normal. I now believe that in many, if not most, of these cases the cause is tuberculosis.

GRENZ RAYS AND THEIR APPLICATION IN OPHTHALMOLOGY

I. THEIR PROPERTIES OF PENETRATION

P. DETHMERS, M.D.

AND

P. H. BOSHOFF, M.D.

LEIDEN, HOLLAND

Grenz rays are widely used in the practice of dermatology as a therapeutic measure. They are used to a limited extent in the field of ophthalmology.

The good results obtained by one of us in the treatment of certain dermatologic diseases and the casuistic reports of favorable results in the treatment of ocular diseases in the recent literature [1] led us to investigate carefully the possibilities of the application of grenz rays in the field of ophthalmology and if possible to arrive at a safe and correct dose of these rays for the treatment of diseases of the eye.

Before observations could be made on the therapeutic effect of these rays, the following problems had to be solved satisfactorily: (1) the degree of absorption in the various tissues of the eye, a factor which largely determines the damaging effects which these rays may have on the delicate and important parts of the eye, and (2) the extent to which the eye is sensitive to irradiation by grenz rays and the possible reactions that may appear.

The first of these problems will be dealt with in this paper, while the second will be dealt with in a subsequent publication. Before proceeding further, we will summarize the main features and biologic effects of the grenz rays in general and then follow with a description of our method of investigation and the results obtained.

1. Thiel, R.: Glaukom, Ztschr. f. Augenh. **81**:178, 1933. Krasso, I.: Die Beeinflussung des Glaukoms durch Allgemein Bestrahlungen mit Bucky Grenzstrahlen, ibid. **69**:74, 1929; Anwendung und Dosierung von Buckys Grenzstrahlen in der Augenheilkunde, Strahlentherapie **38**:358, 1930; Grenzstrahlentherapie der Conjunctivitis acuta und Chronica catarrhalis, Ztschr. f. Augenh. **75**:285, 1931; Die Behandlung von Erkrankungen des vorderen Bulbusabschnittes mit Buckys Grenzstrahlen, Verhandl. d. Ophth. Gesellsch. in Wien, 1930, p. 61; abstracted, Klin. Monatsbl. f. Augenh. **84**:561, 1930. Pfeiffer, R. L.: Treatment of Diseases of the Eye with Grenz Rays, Arch. Ophth. **21**:976 (June) 1939.

MAIN FEATURES OF GRENZ RAYS

Grenz rays were first used therapeutically by Bucky[2] and are often referred to as Bucky rays. They are very soft roentgen rays with a wavelength of approximately 2 to 4 angstrom units, being rays of a wavelength situated between the ordinary roentgen rays and the ultraviolet rays in the electromagnetic spectrum.

Grenz rays are formed in a special tube from which they have their exit by means of a Lindemann window, because these nonpenetrating rays are totally absorbed in the wall of the ordinary roentgen tube. The Lindemann window consists of 0.2 to 0.3 mm. of thick glass, which is constructed from materials of exceptionally low atomic weight.

The quality of grenz rays is determined in the half value layer, which is usually expressed in millimeters of aluminum and depends on the voltage of the current used and on the filtering.

The grenz rays penetrate only the superficial layers of most mediums, a fact which renders not inconsiderable the amount of absorption that takes place at the Lindemann window and in the layer of air which is usually interposed between the apparatus and the object which is irradiated. Bucky[2] compared the amount of absorption in different mediums. At a tension of 10 kilovolts and a half value layer of 0.03 mm. of aluminum, he found an absorption of 40 per cent in 0.5 mm. of human skin, of 70 per cent in 1 mm. of human skin and of 86 per cent in 2 mm. of human skin; he also found half value layer readings in a layer of 0.47 mm. of water, a layer of 0.52 mm. of epidermis and a layer of 0.77 mm. of subcutaneous tissue.

As in the case of roentgen rays, the quantity of grenz rays is also expressed in roentgens. The measurement of the quantity is made relatively simple by the use of dosimeters specially constructed for the purpose. The quantity is dependent on the strength and tension of the current, on the filtering and on the distance at which the object is irradiated.

BIOLOGIC EFFECTS

Grenz rays and other roentgen rays are essentially the same as far as the biologic effects are concerned, except that in the case of grenz rays these effects are totally dependent on the voltage and on the absorption curve in the different tissue layers. As with roentgen rays, one finds erythematous, even bullous, reactions accompanied by some degree of pigmentation. These heal without permanent damage. Only by employing massive doses of many thousand roentgens may one see telangiectasia and atrophy occur. With even higher doses, which are rarely

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2. Bucky, G., cited by Fuhs and Konrad.[3a]

given, epilation may occur. These facts show that Bucky rays when compared to roentgen rays are relatively harmless.

With regard to the reactions after irradiation the well known "wave phenomenon" of the local reactions may be mentioned, whereby during a period of two to five weeks the erythema appears in definite waves. This phenomenon has already often been described by many investigators[3] and has also been observed by us.

Less known in the literature are the general reactions that sometimes appear and which are directly comparable to the malaise after roentgen and radium treatments. Half an hour after treatment there is a sharp decrease in the number of leukocytes in the blood. This has been described by many authors.[4] Hitherto unknown is the "wave phenomenon" of the general reactions, which was discovered by one of us[5] and which will be the subject of a detailed publication later.

This recurrence of certain general symptoms at definite intervals after treatment with grenz rays was first noted in a woman who was hypersensitive to these rays. After a normal irradiation on the inner surface of the thigh, abnormally strong local reactions occurred in waves during four to five weeks at the same time as subjective symptoms of roentgen ray malaise (severe headache and nausea), which were accompanied by rhythmic changes in the daily erythrocyte count, the sugar content of the blood, the pulse pressure and even in the temperature.

These observations, which contribute toward the question of the still unknown causation of roentgen ray malaise, may, according to one of us (P. Dethmers), be explained by a stimulative or rather irritative

3. (*a*) Fuhs, H., and Konrad, J.: Grenzstrahl-Hauttherapie, Berlin, Urban & Schwarzenberg, 1931. (*b*) Koch, F.: Biologische Untersuchungen über Grenzstrahlen, Strahlentherapie **51**:541, 1934. (*c*) Kalz, F.: Grenzstrahlenprobleme, ibid. **54**:96, 1935. (*d*) Kronenberger, P.: Osservazioni fisiche e biologische, con raggi X extramente molli, Boll. Soc. ital. di biol. sper. **9**:1339, 1934; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **51**:414, 1935. (*e*) Wilhelmy, E.: Ueber die Reaktion der Haut auf langwellige Röntgenstrahlen und Kathodestrahlen, Strahlentherapie **55**:489, 1936. (*f*) Leitner, Z. A.: The Physical and Biological Basis of Grenz Ray Therapy, Brit. J. Radiol. **11**:586, 1938.

4. Bucky, G., and Müller, E. F.: Strahlende Energie, Haut und autonomes Nervensystem, München. med. Wchnschr. **72**:883, 1925. Bucky, G.: Grundlinien und Ausblicke der Grenzstrahlentherapie, Strahlentherapie **24**:524, 1927. Böhm, A.: Blutbildveränderungen nach Buckybestrahlungen, ibid. **35**:592, 1930. Eckel, P.: Ueber den Einfluss der Grenzstrahlen auf Leukozytensturz und Blutbild, ibid. **45**:525, 1932. Leitner.[3f]

5. Dethmers, P.: General Reaction to Grenz Rays with Wave Phenomenon, read before Vergadering van Nederlandsche Dermatologen, The Hague, 1939; Nederl. tijdschr. v. geneesk., to be published.

action on the vegetative nervous system. This fact is also borne out by wavelike reactions, consisting of expulsive vomiting or diarrhea which occurred in young children after treatment of hemangiomas with grenz rays.[6] These symptoms are replaced by migrainous attacks in older patients.

That this investigation of general reactions after grenz rays has greatly expanded and increased in value since the treatment of ocular diseases was attempted can easily be understood if one is reminded of the numerous sympathetic nerve endings in the cornea. The knowledge and experience of these hitherto undescribed reactions after grenz rays is of special value in the treatment of the eye, where, as compared to skin, one does not have the clue afforded by the appearance of an erythema in attempting to fix a correct dosage.

Intimate knowledge of the symptoms of reaction and of the course of the reaction waves is not only of importance in gaging the dosage but is essential in determining the time periods between the treatments. Whereas each person must be treated individually with regard to the type of lesion, local and general sensitivity and rhythm in the wave phenomenon, it may be permissible to stress the fact again that proper experience in using these rays is of prime importance in ophthalmology more than in any other field; otherwise, by improper application this promising therapeutic measure may fall into discredit. One should always bear in mind that the grenz rays are still roentgen rays, although they are relatively harmless by virture of their weak penetration into the tissues.

INVESTIGATION OF THE DEGREE OF ABSORPTION

During the last few years grenz rays have been used sporadically in the ophthalmic department of the University of Leiden according to doses recommended in the literature.[7] The doses used by us were about 60 to 70 r at a tension of 10 kilovolts and a half value layer of 0.02 mm. aluminum at a distance of 10 cm. They were repeated a few times only. The negative results and the ever present fear of the effects of the roentgen rays on the eye resulted in the method falling into temporary disuse.

Encouraged by the fact that one of us had, during the last few years, obtained good results with these rays in the field of dermatology and had acquired experience in their use for different dermatologic diseases,[6] we decided to try them again in the treatment of diseases of the eye.

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6. Dethmers, P.: Treatment of Hemangiomas by Means of Infra-Roentgen (Grenz) Rays, Nederl. tijdschr. v. geneesk. **82:**983, 1938.

7. Krasso, I.: Die Behandlung der Erkrankungen des vorderen Bulbus-abschnittes mit Buckys Grenzstrahlen, Ztschr. f. Augenh. **71:**1, 1938.

Before commencing such treatment systematically we considered it necessary to determine the degree of absorption in the different parts of the eye and thus to obtain a clearer idea of the problems of dosage. Independent of the experiments reported in the literature, we started an investigation along lines which we regarded as corresponding to conditions that may be met with in clinical practice.

Owing to the scarcity of normal human material, we chose the pig's eye as being the most suitable for our purpose. Other workers [8] used rabbits' eyes. The correspondence between the pig and the human eye may be seen from the following figures:

	Human Eye [9]	Pig's Eye [10]
Diameter of the eye	24.15 mm.	24.6 mm.
Thickness of the cornea		
Central part	0.8 mm.	1.0 – 1.2 mm.
Peripheral part	1.1 mm.	0.5 – 0.8 mm.
Thickness of the sclera		
Posterior part	0.5 – 1.0 mm.	1.0 – 1.2 mm.
Equatorial part	0.3 – 0.5 mm.	0.5 – 0.8 mm.

Material and Method of Study.—Our work was done on 100 fresh pigs' eyes, and we were fortunate enough to be able to compare our results on the pigs' eyes with those obtained on one normal human eye and the normal cornea of another human eye. Erggelet, who obtained human corneas from operations, reported his results in 1931.[11]

The original Siemens-Reiniger-Veifa grenz ray apparatus with air-cooled tube was used at a tension of 10 kilovolts and a half value layer of 0.02 mm. of aluminum at a distance of 10 cm. from the tissue on the dosimeter. The Strauss-Mekapion dosimeter was used. This instrument, with its special ionization chamber for measurement of grenz rays, is an integrating dosimeter, which consists of the following

8. Krasso, I.: Klinische und histologische Beiträge zur Kenntnis der Tiefenwirkung von Buckys Grenzstrahlen am Auge, Ztschr. f. Augenh. **75**:32, 1932; Experimentelles und Histologisches über den Einfluss einer einmaliges Bestrahlung mit Buckys Grenzstrahlen auf das gesunde Kaninchenauge, ibid. **70**:237, 1930. Mylius, K.: Wirkung von Buckystrahlen (Grenzstrahlen) auf das Auge des Kaninchens, ibid. **64**:316, 1928. Miyahara: Experimentelle Untersuchung über den Einfluss einer einmaliges Bestrahlung mit Buckys Grenzstrahlen auf das gesunde oder vorbehandelte Kaninchenauge, Acta Soc. ophth. japon. **36**:564, 1932; Ueber den Einfluss der wiederholten Bestrahlungen des normalen Kaninchenauges mit Grenzstrahlen, ibid. **36**:612, 1932; Bestrahlungsversuch mit Grenzstrahlen gegen Kaninchensarkom, ibid. **36**:609, 1932.

9. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1932, vol. 1.

10. Martin, P.: Lehrbuch der Anatomie der Haustiere, Stuttgart, Schickhardt and Ebner, 1923, vol. 4, p. 118.

11. Erggelet, H.: Messungen der Durchlässigkeit der brechende Teile des · Auges für Buckysche Grenzstrahlen, Klin. Monatsbl. f. Augenh. **86**:393, 1931.

parts: The two electrodes of the ionization chamber together form a condenser, which becomes negatively charged. Totally dependent on the quantity of entering grenz rays which cause ionization, a sudden discharge occurs after a certain time, directly after which a rapid recharge follows. These discharges correspond to certain quantities of grenz rays which strike the sensitive chamber and are indicated by various signals, such as the flash of a red light, the ringing of a bell or the indication of a dial pointer. With the help of a uranium standard, the precise number of roentgens can be gaged for each discharge, and hence the quantity of roentgens per minute can be calculated. Gaging was not absolutely necessary in our investigation, for here the number of absorbed roentgens was not as important as the absorption expressed in percentages. The results are easily calculated from the time differences obtained before and after interposition of the absorbing medium.

Measurement was done as follows: The opening B (fig. 1), with a diameter of 7 mm., is situated over the measuring chamber A, and through it the grenz rays can enter. This opening was irradiated from a distance of 10 cm., causing ionization in the chamber, with the resultant discharge taking place within a certain

GRENZ RAY TUBE

10 CM.

B

A
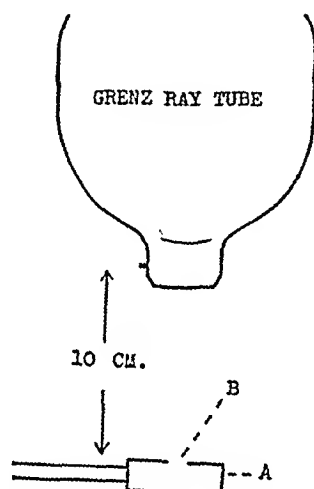
Fig. 1.—Apparatus used for experimental work.

space of time. The time taken for each clearly signaled discharge to occur was measured by a chronometer. The medium to be tested was laid over the opening, B, great care being taken that it covered the opening totally. Under the same conditions it was then irradiated, with the result that fewer discharges occurred, because a large proportion of the rays were filtered off, while each discharge still required the same quantity of roentgens before it took place. To eliminate mistakes produced by changes in the current, the chamber was first irradiated without any material covering it, and the time necessary for the discharge to occur was measured before the next bit of material was put on the dosimeter. To minimize eventual mistakes still further, the average time of five discharges was taken.

From the two findings, (1) the time required for one discharge without the interposing material and (2) the time required for one discharge with the interposing material, one can calculate the absorption in the following way: Let a equal the time in seconds taken for the discharge to occur without the interposing medium; b, the time in seconds taken for the discharge to occur with the interposing medium; R, the amount of grenz rays reaching the uncovered chamber per second and X, the amount of grenz rays absorbed by the medium per second.

Then, the amount of grenz rays reaching the chamber with the interposing medium is

$$(R - X)$$ units per second.

Hence, because the amount required for a discharge remains constant, one gets

$$a.R = b (R - X)$$

from which it follows that

$$\frac{X}{R} = \frac{b - a}{b}$$

$$= \frac{100}{1} \cdot \frac{(b - a)}{b} \quad \text{per cent.}$$

This denotes the percentage of absorption by the interposing medium.

With the help of this simple, yet exact method and the foregoing formula, the percentage of absorption in different mediums could easily be determined.

The different parts of the eye were carefully and cleanly prepared immediately before the experiment, and all possible precautions were taken to prevent drying and absorption of fluid. Thus such factors as drying, absorption of fluid, correct placing of the medium over the opening of the dosimeter and shortening of the time between enucleation and experimentation and between dissection and irradiation should be kept carefully under control if one wants any reliable results in this kind of investigation.

The percentage of absorption for 100 pigs' eyes was determined in the following parts:

1. Cornea { (a) With intact epithelium
           { (b) Denuded of epithelium

2. Sclera { (a) Perilimbic
          { (b) Equatorial

3. Aqueous humor

4. Lens with its capsule

In the human eye the parts investigated were the following:

1. Cornea with intact epithelium
2. Eight different octants of the sclera

ANALYSIS OF RESULTS

The following list contains the percentages of absorption obtained for the corneas and the scleras of the pigs' eyes:

Eye No.	Cornea with Intact Epithelium	Cornea Without Its Epithelium	Sclera: Perilimbic Part	Sclera: Equatorial Part
1	93.5	...	...	...
2	92.0	...	...	...
3	92.0	90.0	...	...
4	90.0	90.0	82.0	...
5	93.0	90.5	77.0	...
6	88.0	89.0	82.0	67.5
7	90.0	92.0	76.0	73.0
8	88.0	87.0	70.0	64.0
9	88.0	87.0	78.5	88.0

Eye No.	Cornea with Intact Epithelium	Cornea Without Its Epithelium	Sclera: Peri-limbic Part	Sclera: Equatorial Part
10	90.0	85.0	78.5	64.0
11	87.0	87.0	70.0	64.0
12	90.5	89.0	80.0	85.0
13	90.0	88.0	71.0	80.0
14	92.0	93.0	88.0	82.0
15	88.0	89.0	75.0	82.0
16	91.0	93.0	·83.0	83.0
17	90.0	...	85.0	87.0
18	92.0	92.0	67.0	85.0
19	92.0	91.0	80.0	75.0
20	92.0	91.0	85.0	85.0
21	97.0	...	88.0	88.0
22	95.0	...	88.0	93.0
23	95.0	...	87.0	83.0
24	93.0	...	87.0	90.0
25	97.0	...	87.0	86.0
26	96.0	...	76.0	84.0
27	94.0	...	81.0	90.0
28	95.0	...	79.0	83.0
29	94.0	...	76.0	86.0
30	94.0	...	84.0	89.0
31	95.0	...	79.0	91.0
32	94.0	...	84.0	75.0
33	95.0	...	86.0	79.0
34	94.0	...	91.0	91.0
35	91.0	...	85.0	90.0
36	87.0	...	70.0	73.0
37	88.0	...	76.0	85.0
38	85.0	...	78.0	70.0
39	91.0	...	78.0	73.0
40	87.0	...	83.0	83.0
41	90.0	...	73.0	84.0
42	88.0	...	70.0	76.0
43	85.0	...	73.0	83.0
44	91.0	...	70.0	87.0
45	88.0	...	76.0	83.0
46	89.0	...	73.0	83.0
47	92.0	...	83.0	85.0
48	88.0	...	83.0	76.0
49	89.0	...	70.0	76.0
50	92.0	...	76.0	86.0
51	91.0	...	90.0	85.0
52	90.0	...	88.0	85.0
53	91.0	...	70.0	74.0
54	90.0	...	76.0	89.0

Eye No.	Cornea with Intact Epithelium	Cornea Without Its Epithelium	Sclera: Peri-limbic Part	Sclera: Equatorial Part
55	91.0	...	74.0	75.0
56	90.0	...	83.0	84.0
57	88.0	...	75.0	85.0
58	88.0	...	76.0	86.0
59	90.0	...	80.0	88.0
60	91.0	...	76.0	87.0
61	91.0	...	75.0	74.0
62	91.0	...	90.0	86.0
63	91.0	...	83.0	81.0
64	92.0	...	74.0	86.0
65	92.0	...	84.0	84.0
66	90.0	...	70.0	70.0
67	89.0	...	83.0	76.0
68	88.0	...	84.0	84.0
69	89.0	...	89.0	76.0
70	92.0	...	70.0	81.0
71	89.0	...	70.0	75.0
72	87.0	...	82.0	84.0
73	89.0	...	78.0	72.0
74	88.0	...	80.0	82.0
75	90.0	...	79.0	72.0
76	90.0	...	72.0	78.0
77	89.0	...	70.0	83.0
78	91.0	...	78.0	83.0
79	90.0	...	·78.0	74.0
80	90.0	...	75.0	77.0
81	90.0	...	72.0	70.0
82	91.0	...	78.0	85.0
83	87.0	...	70.0	75.0
84	92.0	...	74.0	83.0
85	91.0	...	75.0	70.0
86	91.0	...	74.0	80.0
87	89.0	...	76.0	67.0
88	91.0	...	72.0	81.0
89	92.0	...	82.0	80.0
90	91.0	...	79.0	82.0
91	90.0	...	77.0	83.0
92	90.0	...	80.0	83.0
93	91.0	...	77.0	83.0
94	93.0	...	74.0	82.0
95	92.0	...	72.0	77.0
96	90.0	...	78.0	81.0
97	91.0	...	78.0	82.0
98	91.0	...	72.0	86.0
99	89.0	...	80.0	82.0
100	90.0	...	72.0	80.0
101	91.0	...	79.0	86.0
102	89.0	...	74.0	70.0

If one examines these figures more closely, one will immediately notice that there is a great difference in the absorption in the different parts of the eye. Whereas the absorption in the various parts of the cornea differs but slightly, the opposite applies to that of the different

% 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98

CORNEA WITH ITS EPITHELIUM

CORNEA WITHOUT ITS EPITHELIUM

% 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98

PERILIMBIC PART OF SCLERA

EQUATORIAL PART OF SCLERA

% 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98

Fig. 2.—Schematic representation of absorption values.

parts of the sclera. The cornea showed variations between the values of 84 and 98 per cent and the perilimbic part of the sclera between 63 and 94 per cent. These absorption values can be better appreciated from the schematic representation in figure 2, wherein each dot represents a value found.

Cornea.—The absorption in 102 corneas can further be analyzed as follows:

No. of Corneas		Percentage of Absorption
2	....	85
5	....	87
12	....	88
10	....	89
21	....	90
21	....	91
14	....	92
4	....	93
5	....	94
5	....	95
1	....	96
2	....	97

The average absorption was 90.5 per cent.

Sclera.—The schematic representation shows that the absorption in the sclera is subject to a wide range in values. We will not analyze the values for the sclera any further, for the clearness afforded by the schematic representation is sufficient. In comparison to the absorption by the cornea, one may just point out the average values. The absorption by the perilimbic sclera was 77 per cent, and by the equatorial sclera, 79.5 per cent.

In addition to being explained on histologic and anatomic grounds, the widely differing values for the various parts of the sclera may be explained by the possible presence of episcleral tissues and tendon insertions that were unavoidably left behind after the dissection.

If, after the foregoing general study, one regards the absorption values more individually, i. e., the values of each eye as a whole, the following facts will be evident (accepting the average values for cornea, perilimbic part of the sclera and equatorial part of the sclera to be 90, 77 and 79 per cent, respectively) from a study of 97 eyes:

Comparative Values	No. of Eyes
Higher values for both cornea and sclera...................................	35
Lower values for both cornea and sclera....................................	10
Higher values for cornea with lower values for sclera......................	10
Lower values for cornea with higher values for sclera......................	6
Higher values for cornea and equatorial part of sclera with lower values for perilimbic part	17
Higher values for cornea and perilimbic part of sclera with lower values for equatorial part	6
Lower values for cornea and equatorial part of sclera with higher values for perilimbic part	5
Lower values for cornea and perilimbic part of sclera with higher values for equatorial part	8

From this it is clear that although most of the eyes showed a definite relation in the absorption in their different parts, there were many that were far removed from such a norm. It is important to remember that a high value for the cornea need not necessarily mean a high value for the sclera. Still less does a higher value for the perilimbic part of the sclera imply a higher value for the equatorial part or vice versa. To know that some eyes or parts of eyes with absorption values far below the average do exist is of special use in clinical practice. The lowest values found were: cornea, 85 per cent; perilimbic part of sclera, 67 per cent, and equatorial part, 64 per cent.

As far as the absorption in the cornea without its epithelium is concerned, it can be seen from our measurements that the values closely correspond with those of the cornea with intact epithelium, and for this reason we discontinued those measurements. In several cases a cornea without its epithelium showed a higher absorption than the same cornea with its epithelium intact. We have to ascribe this to the imbibition of fluid by the denuded corneas.

Aqueous Humor.—On irradiation of a cornea of known absorbing power, the concavity of which was partly filled with aqueous humor, it was proved that all the grenz rays became absorbed. No signal of a discharge was observed. We are forced to conclude that 100 per cent absorption took place and that the normal aqueous in the eye, being present to an even greater depth than in the experiment, forms an efficient barrier to these rays.

Lens and Its Capsule.—We found the same for the lens and its capsule, where 100 per cent absorption also took place. If these rays ever reach the lens they are capable of considerable damage, for by virtue of their weak penetration they expend all their energy in the parts where they are absorbed.

Human Eye.—Earlier in this paper we mentioned that we were able to compare the results on the pig's eyes with those on the normal human eye. One patient was a girl of 5 years, who in an accident sustained a traumatic perforation situated partly on the cornea and partly on the sclera, and it was considered necessary to enucleate the eye. A part of this cornea was used by a colleague for keratoplasty, while the rest was used by us, with the following results:

Absorption in cornea with intact epithelium...................................90
Absorption in perilimbic part of sclera (upper nasal part)...................81
Absorption in perilimbic part of sclera (upper temporal part)................79
Absorption in perilimbic part of sclera (lower nasal part)...................77
Absorption in perilimbic part of sclera (lower temporal part)...............73
Absorption in equatorial part of sclera (upper nasal part)..................77
Absorption in equatorial part of sclera (upper temporal part)...............79
Absorption in equatorial part of sclera (lower nasal part)..................83
Absorption in equatorial part of sclera (lower temporal part)...............75

The normal cornea of another eye, obtained from a man 47 years of age because of a traumatic perforation, showed 90.5 per cent absorption.

From these values one can see that the human eye and the pig's eyes correspond fairly closely. On considering the average values for the perilimbic and equatorial parts of the sclera, we see that the values of 77.5 and 78.5 per cent for the human eye agreed almost exactly with the average values found for the pig's eye.

CONCLUSIONS AND SUMMARY

We should like to point out that our values listed under perilimbic and equatorial parts of the sclera do not correspond with the anatomic thickness of these parts. This can be ascribed to the fact that it was not the perilimbic part of the sclera only which covered the opening above the dosimeter but that the neighboring thin preequatorial part of the sclera was also irradiated, and hence the lowering of our values relative to the equatorial part. Further, the equatorial part of the sclera also included the thicker postequatorial parts, and this tended to raise the absorption values for the equatorial part. However, we did not attempt to rectify this, since we were trying as much as possible to approach the conditions that will be met with in clinical practice, in which the overlapping of irradiated areas cannot be prevented.

The small percentage of grenz rays at a tension of 10 kilovolts and a half value layer of 0.02 mm. aluminum at a distance of 10 cm. that passes through the cornea will be totally absorbed in the aqueous and will not reach the lens. The ciliary body may be reached by these rays. If one considers the moist conjunctiva, the episcleral tissues and the fluid contained therein and the fluid in the suprachoroidal space, it is doubtful if the quantity of such rays will be sufficient to cause any damage, even if large doses are used. This question can be answered only in practice, and the decision to use large doses should be influenced rather by the nature and gravity of the disease, e. g., if it is malignant, or tuberculosis, the course of the disease and the prognosis, than by the fear of the possibility of doing damage.

It is noteworthy that in some corneas without any epithelium we obtained higher absorption values, a fact which in clinical practice can be applied to swollen corneas in such cases as corneal ulcers, keratitis and corneal abrasions, for the least noticeable fluid absorption markedly affects the transmission of these rays through the tissues.

We are convinced that owing to the great absorption of grenz rays in the tissues the question of their doing damage by penetration is not so important as the question of the general and local sensitivity of the patient concerned. Changes in the quality of the rays, and hence changes in their penetrating properties, naturally modify the foregoing statement to some degree, although the hardness of the rays

obtained by the usual grenz ray apparatus is never such that the penetration becomes a real danger.

The results can be tabulated as follows:

1. In the indicated number of pigs' eyes the average absorption was:
   (*a*) In the cornea..................................... 90.5% (100 eyes)
   (*b*) In the perilimbic part of the sclera................ 77.0% (97 eyes)
   (*c*) In the equatorial part of the sclera................ 79.5% (95 eyes)

2. The range in values was:
   (*a*) In the cornea.................................between 84 and 98%
   (*b*) In the perilimbic part of the sclera...............between 66 and 92%
   (*c*) In the equatorial part of the sclera...............between 63 and 94%

3. The absorption in the aqueous humor placed in the concavity of a cornea of known absorption value was 100%.

4. The absorption in the lens with its capsule was 100%.

5. The values found in the normal human eye, were:
   (*a*) Average absorption in the cornea......................... 90.25%
   (*b*) Absorption in the perilimbic part of the sclera.................77.5%
   (*c*) Absorption in the equatorial part of the sclera................78.5%

VALUE OF TRYPARSAMIDE IN THE TREATMENT OF ATROPHY OF THE OPTIC NERVE DUE TO SYPHILIS

H. SUTHERLAND-CAMPBELL, M.D.

LOS ANGELES

The consideration of amblyopia as it occurs in association with primary atrophy of the optic nerve following tryparsamide therapy is of interest, as within the past two years certain authorities have again advocated the use of this drug for the treatment of neurosyphilis despite the presence of such atrophy. This vacillation in the condemnation and advocacy of a drug is to be expected in view of the fact that tryparsamide is generally conceded to be the most efficacious drug used in the therapy of generalized neurosyphilis, while little is known concerning the mechanism of the production of amblyopia as induced either by syphilis or by the pentavalent arsenical.

Primary atrophy of the optic nerve is probably the most resistant feature of the most resistant form of neurosyphilis, i. e., tabes dorsalis. In earlier days the consensus regarding the value of any form of treatment then extant was pessimistic. When a halt in the degenerative process was manifest it was largely considered to be spontaneous rather than the result of any form of therapy then in use. Much was expected from the arsenicals; but after adequate use of them evidence indicated that the expectations were not to be realized in spite of the more elaborate and intimate methods of administration, as exemplified by the Swift-Ellis mode of procedure.

The earliest of the pentavalent compounds, sodium arsanilate (atoxyl) was first used by Thomas in the treatment of trypanosomiasis, psoriasis and anemia. It was used in the treatment of syphilis after the discovery of Spirochaeta pallida. Not long after its adoption, Bornemann and Igersheimer reported the development of toxic symptoms affecting the optic tract; once the symptoms occurred, blindness appeared inevitable. This caused sodium arsanilate to be discarded by syphilologists in general. Ehrlich next produced a drug, sodium acetylarsenate (arsacetin), which was used only a short time because of its deleterious effect on the optic apparatus. Lorenz and his co-workers [1] next utilized

1. Lorenz, W. F.; Loevenhart, A. S.; Bleckwenn, W. J., and Hodges, F. J.: Therapeutic Use of Tryparsamide in Neurosyphilis, J. A. M. A. **80**:1497-1502 (May 26) 1923.

the synthetic compound known as tryparsamide, which was produced by Jacobs and Heidelberger at the Rockefeller Institute in 1917.

In 1919 Pearce and Brown [2] reported concerning a series of animals they had infected with various strains of trypanosomes and spirochetes. They stated that there was no organic or functional disturbance following therapeutic doses of tryparsamide and that "a definite effect was produced upon the course of the infection by Treponema pallidum . . . and that its chief effect was the peculiar manner in which it modified or controlled the course of the infection."

Since that time reports of the treatment of syphilis in man with tryparsamide have been mainly concerned with its beneficial action in neurosyphilis as compared with the somewhat mediocre results which are obtained in the early and secondary stages of the disease due to its feeble spirocheticidal action. In 1924 Moore, Robinson and Lyman [3] stated that the use of tryparsamide in the treatment of primary, secondary and tertiary syphilis unaccompanied by neurosyphilis was precluded and that most striking clinical results were obtained in patients with meningovascular syphilis. Pearce and Brown [4] later made corroborative and more favorable findings. Much work concerning the minimum lethal dose, arsenic content of the blood, mode of excretion and ability of the drug to penetrate into the spinal canal was done. The latter manifested the opposite results invariably obtained by researchers in the realm of syphilotherapy. Voegtlin, Smith, Dyer and Thompson [5] demonstrated that tryparsamide possesses a high degree of ability to penetrate into the central nervous system. Fordyce and Myers [6] stated that tryparsamide does not possess unusual penetrative power. Cornwall, Bunker and Myers [7] found that the quantity of arsenic in the spinal fluid after the use of silver arsphenamine was three to eight times greater than when tryparsamide was used and from this concluded

2. Pearce, L., and Brown, W. H.: Chemotherapy of Trypanosome and Spirochete Infections, J. Exper. Med. **30**:417, 437, 455 and 483 (Nov.) 1919.

3. Moore, J. E.; Robinson, H. M., and Lyman, R. S.: Results of Tryparsamide Therapy in Syphilis, J. A. M. A. **83**:888-891 (Sept. 20) 1924.

4. Brown, W. H., and Pearce, L.: Present Status of Investigations with Tryparsamide, New York State J. Med. **24**:751-756, 1924.

5. Voegtlin, C.; Smith, M. I.; Dyer, H., and Thompson, J. W.: Penetration of Arsenic into Cerebrospinal Fluid, with Particular Reference to Treatment of Protozoal Infections of Central Nervous System, Pub. Health Rep. **38**:1003-1021 (May 11) 1923.

6. Fordyce, J. A., and Myers, C. N.: Quantitative Studies in Syphilis from a Clinical and Biologic Point of View, Am. J. Syph. **9**:490-501, 1925.

7. Cornwall, L. H.; Bunker, H. A., Jr., and Myers, C. N.: Arsenic in Spinal Fluid: Quantitative Estimation Following Intravenous Administration of Tryparsamide and Silver Arsphenamine, Arch. Neurol. & Psychiat. **25**:137-144 (Jan.) 1931.

that the favorable effects after the use of tryparsamide could not be attributed to the quantity of arsenic entering the spinal fluid.

Tryparsamide at the outset suffered the questioning common to any new compound recommended for use in the therapy of syphilis. It now appears that the earlier pessimism accorded the drug, including its use in the therapy of neurosyphilis, was due to observations made over too short a period. As time passed judgment became more favorable, until today tryparsamide holds the enviable position of being considered almost equal to malaria in the therapy of neurosyphilis. The production of toxic amblyopia in a small proportion of the patients treated with tryparsamide has been of sufficient moment to cause its value to be questioned at intervals, in spite of which it remains in international use today. It must, however, be accepted that this drug is responsible for visual damage in certain cases. This is indicated in papers by Woods and Moore,[8] Fine and Barkan[9] and many others. The statistics of certain of its supporters, on the other hand, tend to indicate that the incidence of visual damage after its use is decidedly low. In the few pathologic reports concerning changes found associated with amblyopia after the use of pentavalent compounds other than tryparsamide, i. e., sodium arsanilate and sodium acetylarsenate, a common observation is that no pathologic changes are to be noted apart from those found in the eyes and optic pathways.

Leinfelder[10] more recently reported on the first pathologic change in a case of tryparsamide amblyopia which occurred within nine days after the administration of 1 Gm. of tryparsamide and seven days after visual symptoms first obtained. The case was classified as one of early primary atrophy of the optic nerve, both eyes manifesting contraction of the fields of vision and reacting to light, although sluggishly. The findings showed that there was acute degeneration of the retinal ganglion cells with acute degeneration of cells in the innermost portion of the inner nuclear layer. There was no evidence of acute primary degeneration in the optic nerves or tracts, and general pathologic changes due to arsenic poisoning were not observed.

The picture as presented cannot be assumed to represent the pathologic changes produced by tryparsamide in the strictest sense of the terms, which would demand certain requirements relative to pretherapeutic negative ocular findings and visual fields. Even in the latter

8. Woods, A. C., and Moore, J. E.: Visual Disturbances Produced by Tryparsamide, J. A. M. A. **82:**2105-2111 (June 28) 1924.

9. Fine, M., and Barkan, H.: Prevention of Ocular Complications in Tryparsamide Therapy, Am. J. Ophth. **20:**45-52 (Jan.) 1937.

10. Leinfelder, P. J.: Pathologic Changes in Amblyopia Following Tryparsamide Therapy, J. A. M. A. **111:**1276-1280 (Oct. 1) 1938.

case, as considered in a syphilitic person, it would be difficult to assert what measure of blindness should be accorded either of the processes under consideration. Beigelman [11] expressed the belief that the optic disks frequently manifest involvement of the peripheral fields by the syphilitic process alone and that this is due to a somewhat chronic form of peripheral neuritis which obtains before the central areas are affected. Scholtz [12] expressed the belief that the preamblyopic phase of tabes can be distinguished from that of the toxic reaction to tryparsamide by an examination of the eyegrounds, as the nerve heads in these two conditions manifest differentiating features. Furthermore, the signs of syphilitic atrophy of the optic nerve are present in cases of tabes long before the amblyopia obtains and may be visualized when the ocular disturbances are first noted, whereas the toxic reaction to tryparsamide is not associated with chronic changes in the eyegrounds. In this regard, Beigelman stated that in his opinion these differentiating features are more theoretic than clinically actual.

The consensus up to the present indicates that toxic reactions to tryparsamide rarely occur if the optic disks are normal and the visual fields unaffected and that the presence of any abnormality in either precludes the use of tryparsamide. Furthermore, it is commonly held that if objectionable reactions occur in the visual apparatus after the use of tryparsamide, the administration should be stopped and no further attempt made to use the drug after a period of rest. It would now appear that the foregoing standard of procedure is being abandoned, as certain ophthalmologists contend that tryparsamide should be employed in spite of the presence of changes in the eyegrounds and constricted fields. Mayer's [13] paper supports the latter contention, as does Cordes [14] in his discussion of Mayer's paper, when he stated that "this series of cases coincides with my experience, that optic atrophy in itself is no contraindication to the use of tryparsamide." Concerning 2 cases reported with a history of blindness after the use of tryparsamide, he stated that as "there was no record of examination of visual acuity, fields or fundus before the therapy was instituted, obviously these cases are of no value in determining the effect of the drug. More large series of carefully controlled and observed cases should be reported so that it will be possible to determine definitely what the contraindications may be to the use of tryparsamide." The foregoing conclusion indicates that the former standard of procedure should be maintained in general practice

11. Beigelman: Personal communication to the author.

12. Scholtz: Personal communication to the author.

13. Mayer, L. L.: Tryparsamide Therapy of Neurosyphilis and Atrophy of Optic Nerve, J. A. M. A. **109**:1793-1796 (Nov. 27) 1937.

14. Cordes, in discussion on Mayer.[13]

until such determining factors are obtained, for while it is agreed that tryparsamide is of benefit in the treatment of generalized syphilis of the nervous system the preponderance of evidence indicates that its action is harmful in the presence of primary atrophy of the optic nerve. It must be accepted that the syphilitic virus and tryparsamide both have an affinity for the optic tract in certain cases. In the case of syphilis the ocular process is a chronic inflammatory one; in the case of the pentavalent arsenical it is apparently a widely varying acute process due to either an allergic or a toxic reaction. Whatever the attribute of the ocular reaction to the drug, one must find room for questioning two extremes in reactivity from a constant cause, for it must be admitted that in general biologic reactions manifest a range of varying clinical pictures, including the intermediate as well as the extreme. What therefore is the explanation of two widely different types of reaction toward a given drug? It is possible that the degree of damage already obtaining may have some influence on the degree of reactivity to the drug; thus in some cases the syphilitic process would be so far advanced that the tryparsamide might produce a fulminating type of reaction. However, this assumption does not answer the question regarding the two extremes in reactivity. It would be more feasible if later data demonstrate that intermediate reactions do occur from tryparsamide but have not as yet been observed or reported.

While it is generally accepted that primary atrophy of the optic nerve occurs in some 20 per cent of tabetic cases and that the condition commonly advances to amblyopia in some two to four years, that the purely syphilitic amblyopic process may sometimes be acute is shown by the following case:

J. P., a white man, aged 27, was admitted to the hospital on Sept. 30, 1937, with the complaints of blurring of vision for the past two days and indigestion, gas and heartburn after eating for past two years. In July 1937 he had burning and pain on urination for three or four days. He stated that he had never had gonorrhea. Seven years previous to his admission a chancre developed approximately three weeks after exposure, a small shallow ulceration which oozed but did not bleed. It was not painful. A physician gave him some mild mercurous chloride to put on, and it healed in six weeks. No secondary rash occurred on the body. The patient has been well since with the exception of indigestion and heartburn after meals for the past two years. Blurring of vision came on suddenly two days before admission. The patient had an artificial right eye. The left eye was fixed and did not react in accommodation or to light. There was incoordination in both arms, more marked in the left. The Romberg sign was manifested by slight swaying. Deep reflexes were present in the arms, knees and achilles tendons. Deep pain sense was markedly diminished. There were no other sensory changes. Atrophy of the optic nerve of the eye was discovered. A diagnosis of tabes dorsalis was made.

General physical examination gave negative results except for neurologic findings.

The Wassermann reaction of the blood was 4 plus.

On October 8 the spinal fluid was clear and colorless. The pressure was 110 mm.; the cell count was 214 per cubic millimeter, and the globulin was markedly increased. The Wassermann reaction was 3 plus. The colloidal gold curve was 5555511000.

The ocular findings were taken from the records of Dr. Rodman Irvine for September 30. Examination showed a blind right eye lost nineteen years previously following an injury. The pupil of the left eye was dilated. It did not react to light. The ocular media was clear; the disk was sharply outlined and pale on the
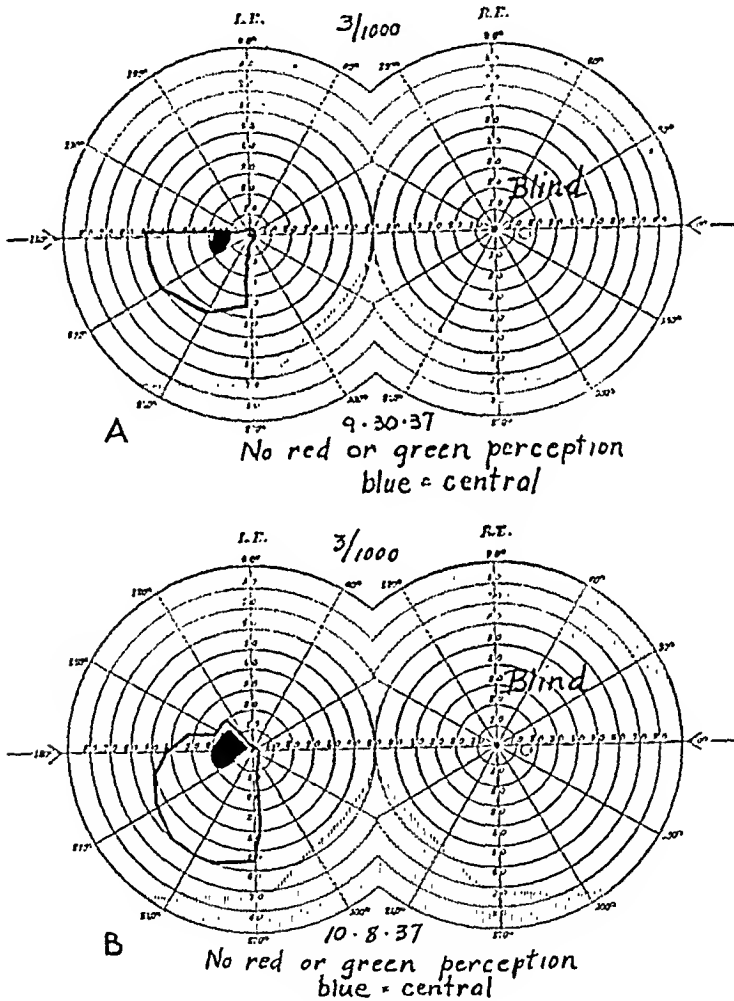
A, visual fields of patient on Sept. 30, 1937. *B*, visual fields on October 8.

temporal side. There was no evidence of any inflammatory reaction. The visual fields showed involvement of all quadrants except the lower temporal, and there was beginning involvement of the fixation area. The patient was unable to see red or green but could see blue only in the central area.

Antisyphilitic therapy was commenced on October 5, with no beneficial result, the patient stating that the rate of increasing blindness was definitely stimulated by the institution of treatment. Within about three weeks the patient became blind, as approximately one month after admission, on November 3, the vision was reduced to recognition of light and forms only.

The commencing form of therapy might be questioned here, as a solution of sodium bismuth iodide and sodium iodide in ethyl glycol was administered intramuscularly; however, the proper mode of procedure under these circumstances is still under question and is mainly the reason for this paper.

Mayer stated that "patients with optic atrophy due to syphilis should have the advantage of tryparsamide when the drug is indicated." The concluding part of this sentence leaves much to be desired on the part of the therapeutist, as the fundamental basis of his problem is contained in the phrase "when the drug is indicated." Is the drug indicated in cases of syphilis associated with primary .atrophy of the optic nerve, in which, of necessity, there is always involvement of the visual field? Lillie,[15] discussing Mayer's paper, observed: "No one has definitely proved that tryparsamide or any other arsenical is neurotropic. The type of field changes occurring before, during or after a proper therapeutic regimen has been instituted are similar to those occurring in untreated syphilis, and as yet no pathognomonic field defect due to tryparsamide has been demonstrated. I believe, as does Mayer, that suggestion plays an important part in the production of subjective symptoms, while the organic changes are best explained by a direct syphilitic process in the optic nerves, namely, a perineuritis. If tryparsamide is of value in arresting active syphilis of the central nervous system it should also be of value in arresting active inflammation of the retina, choroid or optic nerve, and the presence of the latter should be no contraindication to its use." He further stated that the unfavorable prognosis of an untreated active syphilitic process of the visual apparatus requires the use of any antisyphilitic therapeutic agent which might benefit the condition and should be used regardless of the pathologic condition existing when the therapeutic regimen is instituted.

It would appear that there are some who feel that the action of tryparsamide is decidedly neurotropic in certain cases, as the pentavalent arsenicals are known to have produced blindness in nonsyphilitic persons; moreover, Young and Loevenhart[16] demonstrated that both sodium arsanilate and tryparsamide produced optic lesions in rabbits and concluded that the toxic effect of the arsenicals was related to the molecular structure of the compounds and that arsenicals with the amino group in a para position to the arsenic induced such lesions, while arsenicals with the amino group in a meta or ortho position to the arsenic were harmless.

15. Lillie, in discussion on Mayer.[13]

16. Young, A. G., and Loevenhart, A. S.: Relation of Chemical Constitution of Certain Organic Arsenical Compounds to Their Action on Optic Tract, J. Pharmacol. & Exper. Therap. 23:107-126 (March) 1924.

I shall consider other contentions in favor of the use of tryparsamide in the presence of primary atrophy of the optic nerve. It should be used because it benefits active syphilis of the central nervous system. This is debatable, for it might just as readily be contended that arsphenamine should be utilized in a case in which there was marked saccular aneurysm of the aorta or in which there is coronary involvement for somewhat similar reasons; i. e., that it is the best agent one can employ for active syphilis outside the central nervous system. Yet it must be admitted that the Herxheimer reaction might have a grave effect on the lesions in question in the preliminary phase of the healing cycle. For this reason arsphenamine is rarely utilized at the outset in the therapy of tertiary syphilis associated with cardiovascular involvement. Similarly, it is well known that in cases of tertiary syphilis in which the lesions are of long standing and are quiescent the eyes may be aversely affected by the use of arsphenamine.

The drug should be used because statistics show that blindness due to primary atrophy of the optic nerve occurs in about 35 per cent of untreated or inadequately treated syphilitic persons, whereas only some 2 to 10 per cent of persons become blind during treatment with tryparsamide. This suggests that tryparsamide is preventing the development of blindness sufficiently marked to affect the central visual acuity in about 25 per cent of the cases.

This suggestion fairly warrants questioning. In effect, it is stated that because only 2 to 10 per cent of persons under treatment with tryparsamide become blind, the suggestion is in order that tryparsamide is preventing blindness in the remaining 25 per cent. Primarily, it would appear reasonable to eliminate the percentage of the 35 per cent cited which includes inadequately treated patients, since such patients should find no place in the equation, and it could fairly be assumed that blindness would occur just as readily if the patients had been inadequately treated with tryparsamide. Secondly, the phrase "whereas only some 2 to 10 per cent of persons become blind during treatment with tryparsamide" appears to embrace a modicum of misleading ambiguity. Surely these figures cannot be concerned with the number of patients who become blind after the course of treatment with tryparsamide is ended, in which case it becomes mandatory for comparative purposes that one consider only those persons blinded by syphilis during the same period of time as is occupied by the course of tryparsamide therapy. Tabes is notoriously resistant to treatment, yet in its own economy one sees apparent phases of beneficial change in certain cases. More commonly a halt in the degenerative phenomena is seen, and this sometimes obtains for such long periods that it is often presumed that the disease process has died out. Under these circumstances it becomes difficult to determine

what degree of benefit may be attributed to a given therapeutic agent. I believe that the most optimistic therapeutist of experience hopes for little more than arrest of the process in primary atrophy of the optic nerve, and when this apparently occurs, it is accepted more in the nature of an interlude than a conclusion. For this reason the length of time the tabetic patient with primary atrophy of the optic nerve is treated varies largely, intermittent therapy usually continuing throughout life.

Behr [17] stated that it is difficult to evaluate therapeutic measures in tabetic atrophy of the optic nerve; as the atrophy, in common with other tabetic symptoms, may have longer or shorter remissions without any recognizable cause and as the tabes associated with atrophy of the optic nerve is usually of the mild type, such remissions and apparent improvements are to be expected. Spontaneous regression also occurs but is rare, while loss of vision in the course of two or three months is extremely unusual. Behr's contraindications to the use of tryparsamide are: diminished central acuity, loss of color fields even with normal form, constricted color and form with normal central, transient visual disturbance of form and photopia.

A complicating and little considered factor in any attempt to determine the effectiveness of any therapeutic agent in this disease is the influence of time on its clinical manifestations. Barkan [18] called attention some years ago to the difference in the clinical teaching material coming to hand over a period of little more than a decade; this change he attributed to modern serologic and therapeutic agents. However, observations of a similar nature, made by Fracastor at a time when mercury and guaiacum were the only known therapeutic agents, indicate that immunologic qualities play the major role in the metamorphosis of the clinical lesions of syphilis.

It has been observed that no pathognomonic field defect can be attributed to tryparsamide. A similar statement could be made regarding syphilis, and it can be accepted that both field defects and pathologic manifestations as they result from the disease or the drug will remain for some time an academic study of major proportions. In view of this, the more informative clinical reactivity will be considered. According to the observations of several authorities, who have reported the occurrence of amblyopia in certain patients with syphilis of the central nervous system under therapy with tryparsamide, these patients invariably manifested involvement of the visual fields prior to treatment, some 20 per cent more persons were affected by permanent damage to the optic nerve

17. Behr, C.: Ueber die anatomischen Grundlagen und über die Behandlung der tabischen Sehnervenatrophie, München. med. Wchnschr. **73**:311-313 (Feb. 19) 1926.

18. Barkan, H.: Ocular Syphilis: Its Treatment, California & West. Med. **45**:13-16 (July) 1936.

if visual field defects were present prior to treatment than when no findings could be made previous to therapy, when approximately 2.9 per cent were affected, and two types of morbid reactivity occurred. The first, and the commonest type, was characterized by visual symptoms after four to six injections; blindness ensued only if the therapy was continued, and cessation of therapy resulted in a fairly rapid clearing of the visual symptoms. The second type, a fulminating variety, was characterized by visual symptoms and rapidly developing blindness irrespective of cessation of therapy.

Considering the latter type first, it cannot be denied that amblyopia occurring within a few days after visual symptoms is decidedly foreign to the syphilitic process alone yet is met with in persons undergoing therapy with tryparsamide in sufficient numbers to be reported on; furthermore, in the former larger group blindness only results if the use of the drug is continued after the development of visual symptoms, and the symptoms clear up with the discontinuance of the drug. These facts are tenable evidence of the culpability of the drug, and under such circumstances it seems illogical to persist in the use of tryparsamide in the presence of primary atrophy of the optic nerve, especially when the most to be expected from its use is the questionable prevention of the advance of the morbid process for a varying period of time. In any event, the view that because of the threat of blindness a person should be subjected to a drug which is as doubtfully effective in some instances as it is dangerous in others is hardly in order, for its effectiveness in primary atrophy of the optic nerve is questioned, while its danger is in general admitted.

In discussing Barkan's paper [18] I observed that in the therapy of syphilis of the eye "collaboration in the therapy of ocular syphilis between the syphilologist and the ophthalmologist becomes more of a necessity than an adventure." The extreme views held at this later date by some of the leaders of both these branches of medicine lend a modicum of weight to the observation. In Moore's [19] text on syphilotherapy one finds the following statement: "Tryparsamide in syphilis of the eye. . . . This drug is of no value in the exudative and inflammatory lesions involving the external coats of the eye. Its only field of usefulness is in neurosyphilis. Here, however, it may not be used with safety where there is involvement of the optic nerve or retina. Woods and I have shown that the incidence of symptoms of intolerance following its use is much greater in patients with preexisting visual damage, and under these circumstances there is grave risk of toxic amblyopia and permanent blindness." A further observation by the same author is as follows:

19. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933, pp. 316 and 325.

"The only occasion in which the use of tryparsamide is justified in optic atrophy is when the patient is already completely blind. Under these circumstances it may, of course, be used freely and is a most valuable drug for the management of the generalised neurosyphilis."

Whatever measures are eventually adopted in the treatment of primary atrophy of the optic nerve, I believe that tryparsamide stands condemned, as in the available literature but 7 reports, with a relatively small total number of cases, are concerned with the treatment of primary atrophy of the optic nerve with tryparsamide without damage to the optic system; and in the discussion of one of the reports, a case was included in which the patient seemed to have been aversely affected by the tryparsamide. Only 3 of the reports indicate there was improved vision in a few cases. In practically all other reports covering the greater preponderance of cases, the harmful effect of tryparsamide in the presence of primary atrophy of the optic nerve is contended and maintained, and it appears that the considered opinion of the majority indicates that the use of tryparsamide in the relatively few cases of tabes or of paresis of the tabetic type in which primary atrophy of the optic nerve occurs is not justified in the light of its dangerous potentialities.

The latter view is concurred in by certain general practitioners who have utilized tryparsamide in the presence of primary atrophy of the optic nerve as has sometime been advised.

INTRACELLULAR BODIES OF THE CONJUNCTIVAL EPITHELIAL CELLS

ALSON BRALEY, M.D.

DETROIT

Since the discovery of the inclusion bodies of trachoma by Halberstaedter and Prowazek[1] in 1907, the nature and the significance of intracellular bodies found in conjunctival epithelium have been the subjects of extensive investigation. In 1909 Stargardt[2] reported finding bodies similar to those described by Halberstaedter and Prowazek in an infant with gonococci-free blennorrhea, and later, in cases of gonorrheal blennorrhea, Heymann[3] found large numbers of the same bodies and considered them to be products of the gonococci. Wolbach and McKee,[4] McKee,[5] Isabolinsky and Spassky,[6] Lumbroso,[7] W. S. and P. M. Duke-Elder[8] and others described so-called inclusion bodies in normal or slightly damaged conjunctival cells, and later Gifford and Lazar[9] reported chemically induced inclusion bodies in the conjunctival epithelial cells of guinea pigs. From time to time many of these capable workers have retracted or amended their reports, however, and there seems to be confusion in the minds of many ophthalmologists as to the precise role these bodies should play in the microscopic diagnosis of conjunctival disease and doubt as to the best means of taking, staining and examining epithelial scrapings for diagnostic purposes. The present report was prepared in an effort to clarify this confusion.

1. Halberstaedter, K., and von Prowazek, S.: Deutsche med. Wchnschr. 33: 1285, 1907.

2. Stargardt, K.: Arch. f. Ophth. 69:525, 1909.

3. Heymann, B.: Deutsche med. Wchnschr. 47:663, 1910.

4. Wolbach, S. B., and McKee, S. H.: J. M. Research 24:259, 1911.

5. McKee, S. H.: Ophth. Rec. 20:292, 1910.

6. Isabolinsky, M., and Spassky, W.: Ztschr. f. Augenh. 29:109, 1913.

7. Lumbroso, U.: Arch. Inst. Pasteur de Tunis 13:203, 1924.

8. Duke-Elder, W. S., and Duke-Elder, P. M.: Brit. J. Ophth. 13:1, 1929.

9. Gifford, S. R., and Lazar, N. K.: Inclusion Bodies in Artificially Induced Conjunctivitis, Arch. Ophth. 4:468 (Oct.) 1930.

PROCEDURE FOR DIFFERENTIAL DIAGNOSIS OF
INTRACELLULAR BODIES

Taking the Scraping.—An epithelial scraping from the conjunctiva may be taken in a number of ways. A spatula made from a short length of no. 14 or no. 16 platinum wire is the most convenient implement because it can be heated in a flame and used repeatedly, but a sterile chalazion curet is also satisfactory. After the surface discharge has been removed, the lower conjunctiva should be scraped and the material obtained spread on the lower portion of a glass slide, which is marked L with a glass-marking pencil. The upper lid is everted and a scraping obtained from the upper edge of the tarsus and retrotarsal fold. This material is spread on the upper portion of the same slide, which is marked U. The significance of this differentiation of the source of the material will appear later in the discussion of the inclusion bodies of trachoma and inclusion conjunctivitis.

Staining.—For quick staining, which is especially desirable if the scraping is to be examined while the patient is in the office, several drops of Wright's stain may be dropped on the slide and allowed to remain for from one to three minutes; the slide is then flooded with distilled water and allowed to stain for five minutes, when it may be washed off and examined. Wright's stain, however, does not give quite as clear a differentiation of the cells as the Giemsa method of staining, and control scrapings should be stained by this method whenever any doubt exists. According to the Giemsa method, the preparations are fixed in absolute methyl alcohol for from one-half to two hours and are then dried and stained in a freshly prepared mixture of stock Giemsa stain and neutral distilled water (15 to 20 drops of stain in 40 cc. of water) for one hour before being washed and examined. If on examination the cells are found to be too deeply stained or if the stain has precipitated on the surface of the slide, a wash in 95 per cent alcohol removes the excess stain.

Examination.—The systematic examination of a scraping is most important. Best results are obtained with a microscope having a mechanical stage and fitted with a $\times 15$ eyepiece. The examination is begun under low power ($\times 10$) in the upper left hand corner of the slide and progresses from left to right. If any cells show changes in the cytoplasm, a small amount of immersion oil or liquid petrolatum should be placed on the slide and the cells in question viewed under the oil immersion lens. The examination of the slide is continued from left to right, then back at a lower level from right to left, then back at a lower level from left to right and so on until the entire slide has been examined and every suspicious cell examined under an oil immersion lens. A practiced observer can examine a slide in from three to five minutes.

INCLUSION BODIES OF TRACHOMA AND INCLUSION CONJUNCTIVITIS

There are several virus diseases of the conjunctiva in which inclusion bodies have been demonstrated, but the only two for which they have diagnostic significance at the present time are trachoma and inclusion conjunctivitis.[10] In these two diseases the inclusion bodies are known to represent virus colonies and are of two types, the initial inclusion body

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10. Thygeson, P.: Viruses and Virus Diseases of the Eye, Arch. Ophth., to be published.

and the elementary inclusion body. The elementary inclusion body is the easier to identify, appearing typically as an intracytoplasmic mass composed of uniformly-sized, purple-staining granules in a relatively clear matrix (fig. 1 *A*). This matrix has been shown by Rice [11] and Thygeson [12] to be composed of a glycogen-like substance easily stained with iodine; they have also shown that dilute compound solution of
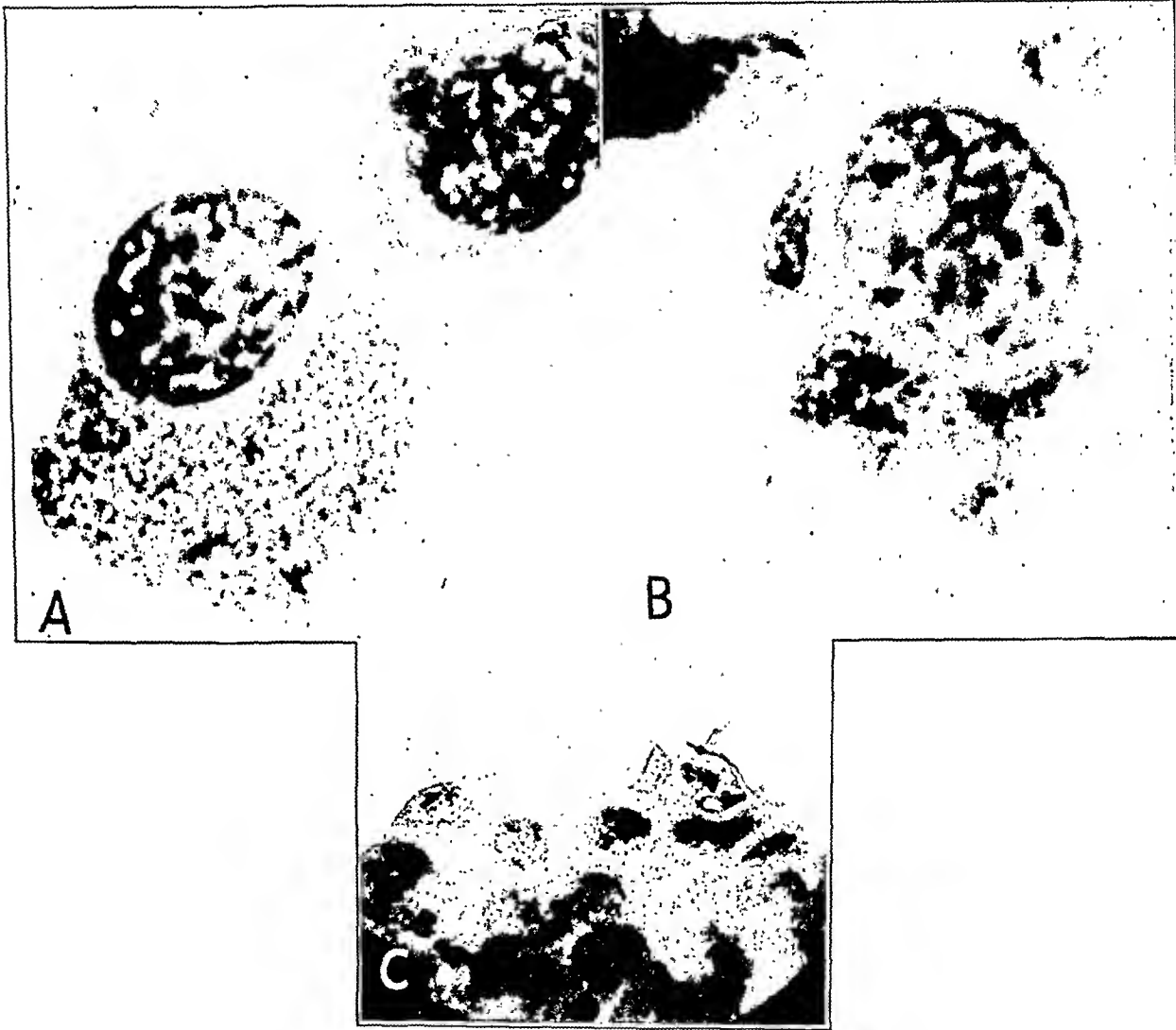
Fig. 1.—*A*, an elementary inclusion body in a conjunctival epithelial cell from trachomatous scrapings. *B*, an initial inclusion body in a conjunctival epithelial cell from trachomatous scrapings. *C*, a trachoma inclusion body in section.

iodine may be used to stain epithelial smears in cases of suspected trachoma or inclusion blennorrhea. With iodine stain the elementary inclusion bodies are deep golden brown, while the cytoplasm and faintly staining nucleus are pale yellow. This means of identifying the

11. Rice, C. E.: Am. J. Ophth. **19**:1, 1936.
12. Thygeson, P.: Am. J. Path. **14**:455, 1938.

inclusion bodies of trachoma and inclusion conjunctivitis, while excellent in experienced hands, must be checked by the Giemsa method, since goblet cells when stained with iodine show a brown-staining spherical mass in the cytoplasm which might confuse the diagnosis.

The initial inclusion body of trachoma and inclusion conjunctivitis is composed of one or more large, blue-staining bodies in the cytoplasm of the conjunctival epithelial cell (fig. 1 *B*). These bodies, first described by Lindner,[13] vary in size, shape and density of staining. They are usually round or oval and are approximately the size of an individual coccus of hemolytic streptococcus. When initial inclusion bodies are found, elementary inclusion bodies and mixed inclusion bodies (composed of both elementary and initial bodies) are usually also present. Inclusion bodies of both elementary and initial body types are also found in stained sections of conjunctival scrapings taken for biopsy in which they are seen in the conjunctival epithelial cells but not in the underlying subconjunctiva or in the mature follicles (fig. 1 *C*).

In the majority of cases a diagnosis of trachoma is indicated if typical inclusions are found in scrapings from the upper lid but few or none in scrapings from the lower lid, and conversely, if most of the inclusions are found in scrapings from the lower lid with few or none from the upper lid, a diagnosis of inclusion conjunctivitis is indicated.

OTHER INTRACELLULAR BODIES

Unfortunately several other types of intracellular bodies which can be confused with virus inclusions occur in conjunctival epithelial cells. A number of these are normal structural alterations in the epithelial cell.

Mitochondria.—All normal epithelial cells contain granules called mitochondria. They appear to play an important role in the physiology of the cells and are constantly undergoing morphologic changes, which can be observed on dark field examination [14] (fig. 2 *A*) or in studies of tissue culture cells. When the cells are young the mitochondria are fine, dustlike particles which are difficult to stain with ordinary methods, taking a faint blue with both the Giemsa and the Wright stain (fig. 2 *B* and *C*). Close examination shows them to be irregular and for the most part slightly enongated. In older cells the mitochondria are coarser and stain more deeply, and when variations in morphologic structure and staining reactions occur in a single cell they may assume the appearance of an inclusion body (fig. 3 *A* and *B*). Differentiation from the elementary inclusion bodies of trachoma or inclusion blennorrhea, however, can readily be made from the somewhat diffuse,

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13. Lindner, K.: Arch. Ophth. **76:**559, 1910.
14. Braley, A. E.: Rickettsia Question in Trachoma: Microscopic Observation on Virus, Arch. Ophth. **21:**735 (May) 1939.

irregular appearance of the mitochondria granules as compared to the discrete elementary bodies of the virus inclusions. Furthermore, the mitochondria are quickly destained with alcohol, while the elementary bodies are alcohol-fast.

Red-staining intracellular bodies of variable size are occasionally encountered. They are much more common in old cultures than in
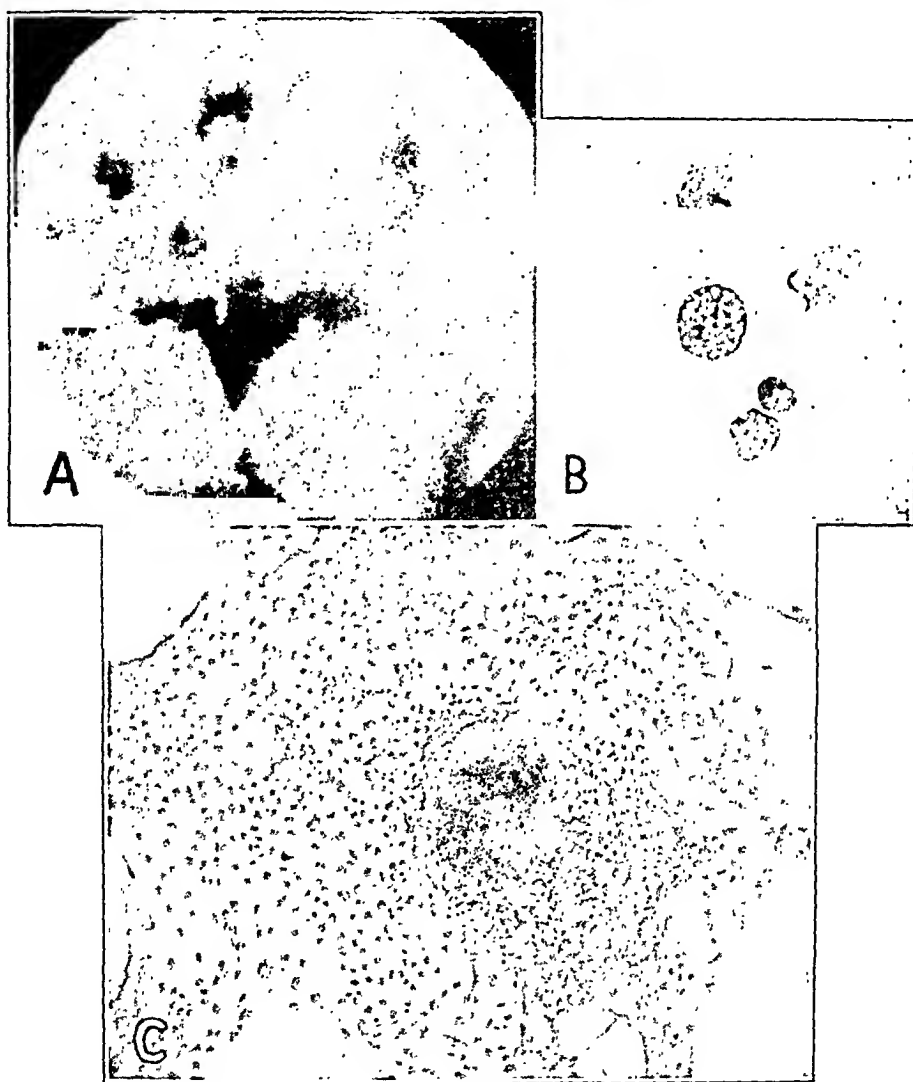
Fig. 2.—*A*, mitochondria as shown by dark field illumination. *B*, an epithelial cell from conjunctiva, containing dustlike granules. *C*, dustlike granules in an epithelial cell grown in tissue culture.

young and appear to be closely allied to keratin [14] (fig. 3 *C* and *D*). They are produced by a coalition of mitochondria, and it is possible to produce them in epithelial cells grown in tissue culture by limiting the amount of dextrose in the media or by allowing the culture to continue to grow without transplanting or changing the media. They represent physiologic changes in the cytoplasm and occur most frequently in the

presence of a chronic irritant. When massed together they may take on the appearance of an initial inclusion body but may be differentiated on the basis of their red color and the marked variation in size of the particles.

Goblet Cells.—The normal conjunctival epithelium contains varying numbers of goblet cells. They occur most frequently in the fornices and on the bulbar conjunctiva but are occasionally seen in the scrapings from the upper edge of the tarsus. When the preparations are somewhat
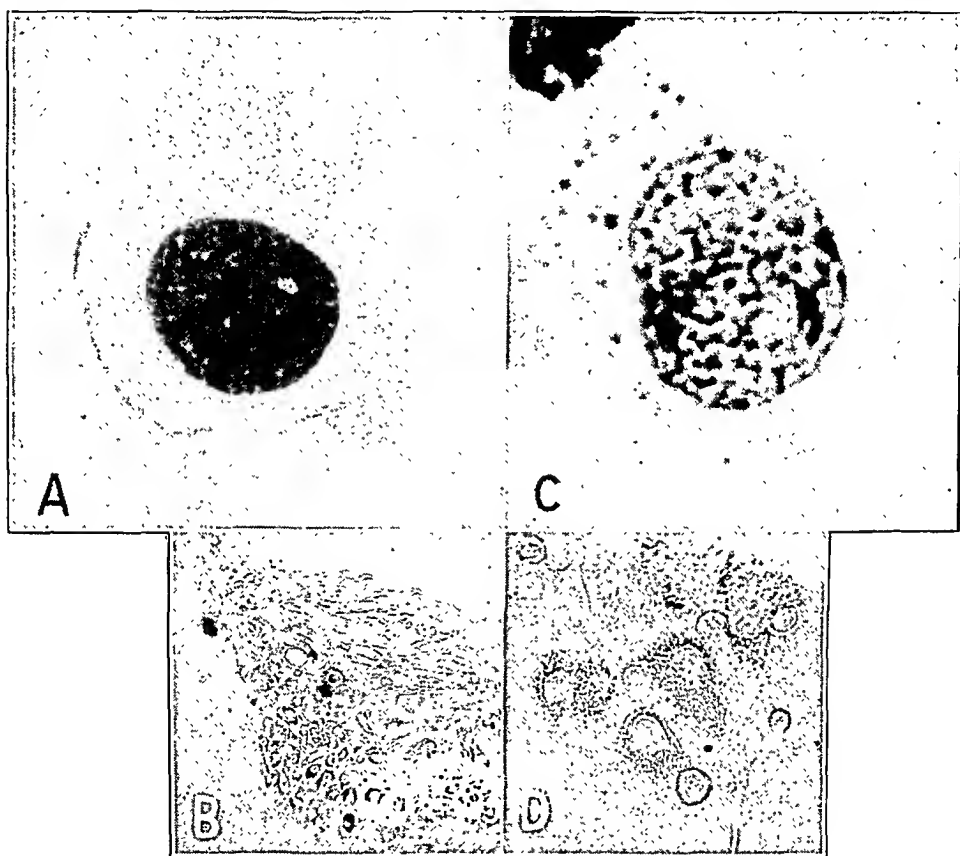
Fig. 3.—*A*, a pseudo inclusion body formed by mitochondria from a conjunctival smear. *B*, a pseudo inclusion body joined by mitochondria in tissue culture. *C*, keratin granules in conjunctival smears. *D*, keratin granules in conjunctival epithelial cells grown in tissue culture.

overstained with the Giemsa stain these goblet cells show homogeneous blue masses in their cytoplasm (fig. 4 *A* and *B*). These could be confused with virus inclusions but are eliminated if the slide is destained in alcohol.

In histologic sections, goblet cells are often seen and can be identified by the fact that their nuclei have been displaced eccentrically by spherical or oval-shaped masses or vacuoles. In preparing histologic sections, the

mucus of the goblet cell undergoes marked changes in character and may appear as a granular mass which could be mistaken for a virus inclusion but for its poor staining qualities.

Melanin Pigment.—Granules of melanin pigment sometimes occur in small numbers scattered through the cytoplasm of conjunctival epithelial cells (fig. 4 *D*). Occasionally they are sufficiently massed
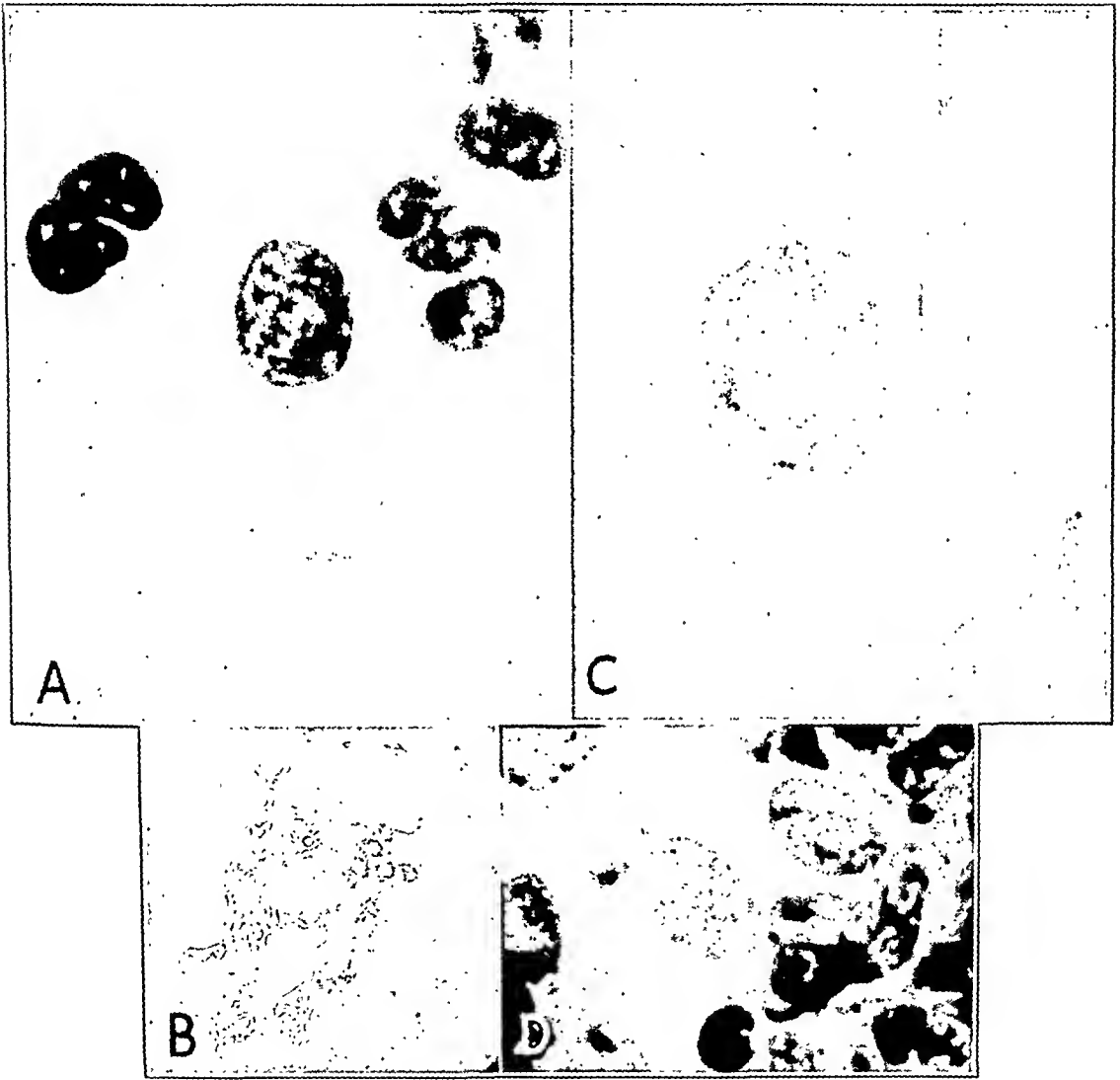
Fig. 4.—*A*, goblet cells from conjunctival smears. *B*, goblet cells in tissue culture epithelium. *C*, nuclear extrusions in conjunctival epithelial cells. *D*, melanin pigment in conjunctival epithelial cells.

to take on the appearance of an initial inclusion body when viewed under low power magnification. Under the oil immersion lens, however, they may be differentiated on the basis of color: The pigment is deep brown when unstained but takes on a distinctly greenish cast in stained preparations. Melanin is sometimes found in conjunctival epithelial cells grown in tissue culture.

Nuclear Chromatin.—One of the commonest intracellular bodies encountered in conjunctival epithelial preparations is produced by extrusion of nuclear chromatin into the cytoplasm of a cell (fig. 4 C). In taking the scraping, a few of the epithelial nuclei are always broken, especially those of young cells. If the nuclear "membrane" ruptures at one point, a small nuclear body may be extruded into the cytoplasm adjacent to the nucleus. When viewed under the oil immersion lens, these bodies are easily identified as being composed of chromatin.

Phagocytosed Cellular Debris.—A most interesting group of intra-cellular bodies are those composed of phagocytosed cellular debris. In
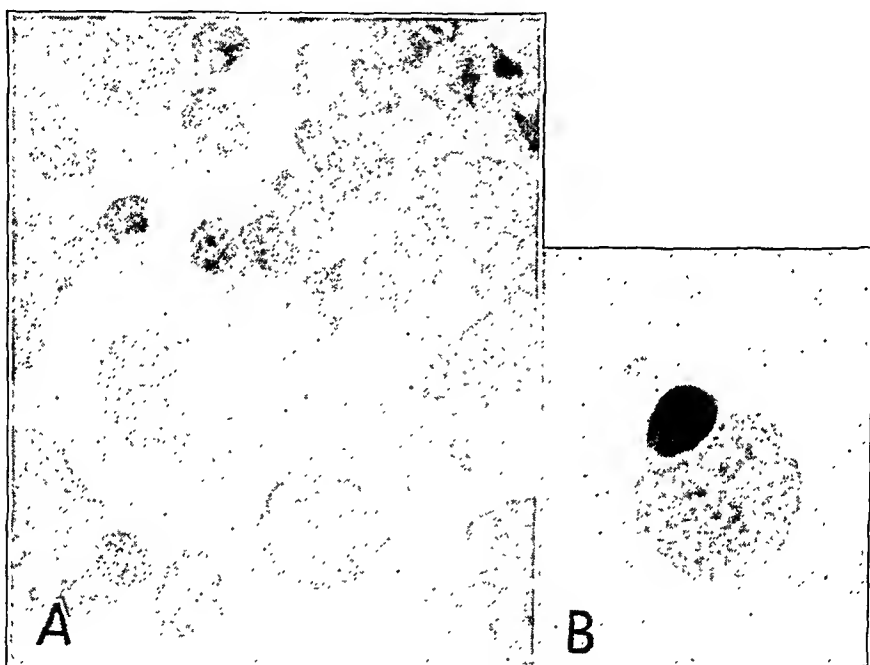
Fig. 5.—*A*, Leber cell with phagocytosed nuclear debris. *B*, conjunctival epithelial cell containing nuclear debris.

some conjunctival diseases in which there is tissue necrosis, notably in trachoma, phagocytosis of necrotic material is always taking place, most of it by the subepithelial histiocytes, which are known as Leber cells when laden with necrotic nuclear material (fig. 5 A). The large polygonal epithelial cells just above the basal layer of the conjunctiva frequently become phagocytic ánd take up parts of nuclear material from dead polymorphic leukocytes (fig. 5 B). The necrotic nuclear debris usually stains uniformly dark blue with clear circumscribed borders. Occasionally spherical, red-staining bodies known as "Russell bodies" are found in epithelial cells and histiocytes. When these are present, plasmacytoids and degenerating plasma cells are seen. The plasmacytoid is a cell with a round, "clock-faced" nucleus and small red-staining

granules in the cytoplasm. There should be no difficulty in differentiating any of these forms from virus inclusions under the oil immersion lens.

Extracellular Bacteria.—Staphylococci and other bacteria may accumulate on the surface of epithelial cells and produce the illusion of intracellular bodies suggestive of the initial bodies of trachoma and inclusion conjunctivitis. However, wherever initial bodies are found elementary bodies will also be in evidence, and these are too small to be confused with bacteria.

SUMMARY

The examination of stained preparations of conjunctival epithelial scrapings reveal the inclusion bodies of trachoma and inclusion conjunctivitis as discrete blue or purple bodies. Intracellular bodies consisting of mitochondria, pigment, keratin, mucin from goblet cells, nuclear extrusions, phagocytosed cellular debris and extracellular bacteria are described, and methods of making, staining and examining scrapings are presented.

ABSTRACT OF DISCUSSION

DR. PHILLIPS THYGESON, New York: Dr. Braley is performing a valuable service in clarifying the subject of the epithelial cell inclusion bodies of the conjunctiva, since many workers have encountered difficulty in the finding and identification of these bodies. It is my opinion that no study of conjunctivitis and keratitis is complete without a microscopic study of epithelial scrapings, and it is to be hoped that all laboratories doing ocular work will become familiar with the technic of inclusion body examination.

It is perhaps well to emphasize again that while the inclusions of trachoma and inclusion conjunctivitis are the only specific virus inclusions of the conjunctiva encountered at all commonly, other virus bodies have been found on rare occasions. In addition to the virus diseases mentioned by Dr. Braley, other diseases, including herpes zoster, varicella, smallpox and lymphogranuloma venereum, may affect the conjunctiva. Of the inclusions of these diseases, only the cytoplasmic inclusions of lymphogranuloma venereum could be confused with those of trachoma and inclusion conjunctivitis. In view of the increasing number of ocular infections reported as caused by this virus, it would not be surprising to encounter these inclusions in epithelial scrapings or in biopsy specimens.

Whereas the finding of inclusion bodies in material from the eyes of newborn infants with inclusion blennorrhea is extremely easy, owing to their abundance, the search for these bodies in material from the eyes of persons with chronic trachoma and adult inclusion conjunctivitis may be tedious, owing to their relative scarcity. Lindner attempted to facilitate the recognition of these bodies by a contrast stain which colored the initial bodies, predominant in young inclusion bodies, blue while the cytoplasm of the cell stained red. This stain, however, has not been satisfactory in my hands for the recognition of the inclusions made up predominantly of elementary bodies, and I prefer the method of Rice in which compound solution of iodine is used to stain the

carbohydrate matrix of the inclusion body. When sufficient material from each case is available, the iodine stain would appear the one of choice, since slides can be covered under low power magnification with great rapidity owing to the high degree of contrast between the brownish red inclusion mass and the pale yellow background.

Under the oil immersion lens the iodine-stained inclusion bodies appear to be full of holes of varying size due to the fact that the component elementary and initial granules fail to stain, an appearance not to be confused with the diffuse brown stain of goblet cells or the faint brown stippling of the cytoplasm of polymorphonuclear leukocytes. The iodine stain also has the distinct advantage that, when desired, the slide can be decolorized in water and restained with Giemsa's stain.

Dr. Braley has not mentioned the fact that the finding of free inclusion body components, the elementary and initial bodies liberated from ruptured inclusions, can also be used for diagnosis. When present together these free bodies give an accurate diagnosis, but a certain amount of training is required before they can be recognized with facility.

Dr. Braley has suggested a method for the microscopic differentiation of trachoma from inclusion conjunctivitis, but it would seem to me that a more accurate differentiation can be made by the study of expressed follicular material. In the trachoma follicle, chromatin-loaded phagocytes or Leber cells are usually abundant, since cell necrosis leading to cicatrization is the principal feature of the disease. Cell necrosis is not present in the follicles of inclusion conjunctivitis, and consequently, Leber cells, if present at all, are scarce.

Further findings of differential value present in the trachomatous material and absent in the material of inclusion conjunctivitis include scattered cell debris and a predominance of large mononuclear over small mononuclear cells, with poorly staining nuclei and often fragmented cytoplasm in the former.

HYPERTELORISM

MILTON L. BERLINER, M.D.

AND

SAMUEL GARTNER, M.D.

NEW YORK

Hypertelorism is a congenital anomaly of the skull and face characterized by a wide separation of the orbits, causing the eyes to be far apart. The large interpupillary distance is exaggerated by a divergent squint in most cases. The anomaly produces an animal-like appearance of the face.

The earliest picture we could find of a person with a condition resembling hypertelorism was published in 1586 by Giovanni Battista della Porta [1] in his book, "De humana physiognomonia" (fig. 1). The drawing of a cow is shown alongside for comparison. The eyes of both the human subject and the cow are far apart and seem to look in opposite directions. This picture was reproduced in 1625 by Samuel Fuchs [2] and again in 1938 by Bojlén and Brems. [3]

Two cases of what appears to be hypertelorism were reported by Sophus Schack [4] in 1858. In 1890 Fridolin [5] described a similar condition as a variety of plagiocephaly. In 1910 Hutchison [6] reported a case of oxycephaly, in which the condition definitely was hypertelorism.

In 1934 Greig [7] made a classic study of 2 cases, in 1 of which autopsy was performed. He realized that he had a new syndrome, hitherto undefined. He named it ocular hypertelorism, a word compounded from the Greek, meaning too far apart. Anatomically, he found the lesser wings of the sphenoid bone were enormously enlarged;

1. della Porta, G. B.: De humana physiognomonia, 1586, p. 189; Nanau, G. Antonius, 1593. The 1586 edition of this work is in the library of the New York Academy of Medicine and the 1593 edition in the Surgeon General's Library.

2. Fuchs (Fuchsius), S.: Metoposcopia et ophthalmoscopia, Argentinae, T. Glaserus, 1615, p. 25.

3. Bojlén, K., and Brems, T.: Hypertelorism (Greig), Acta path. et microbiol. Scandinav. 15:217, 1938.

4. Schack, S.: Physiognomonische Studier, 1858, p. 59.

5. Fridolin, J.: Ueber abnorme Schädel, Virchows Arch. f. path. Anat. 122: 528, 1890.

6. Hutchison, R.: Three Cases of Oxycephaly, Proc. Roy. Soc. Med. (Sect. Dis. Child.) 10:1 and 125, 1909.

7. Greig, D. M.: Hypertelorism, Edinburgh M. J. 31:560, 1924.

he believed this to be the fundamental defect. Subsequent studies, including a second autopsy by Bojlén and Brems,[3] confirmed this belief.

Since 1924 reports of 56 cases have been published. A critical survey by Bojlén and Brems [3] indicated that the condition in 14 was not hypertelorism. They ruled out cases in which the eyes were far apart secondarily to other disorders, such as frontal meningocele or encephalocele.[8] Some cases of congenital nasal and facial cleft have been called cases of hypertelorism, but in these instances the wide inter-ocular distance was secondary to some other condition.

Fig. 1.—Hypertelorism. (From G. B. della Porta: De humana physiognomonia, 1586.)

The reports concerning this anomaly have come from all parts of the world. Many were described by pediatricians, who saw these patients early. As far as we could determine, only 1 other case was reported from an ophthalmologic point of view.[9] This is odd, as the ocular deformity is its most striking characteristic. Consequently, it was felt that this syndrome should be drawn to the attention of ophthalmologists, with the hope that their interest might add some new data concerning this unusual condition.

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8. Oldfield, M. C.: Encephalocele Associated with Hypertelorism, Brit. J. Surg. 25:757, 1938.

9. Weeks, W.: Ocular Hypertelorism, Arch. Ophth. 20:683 (Oct.) 1938.

The physical development and mentality of persons with hypertelorism may be normal or defective. Some show other deformities,[10] such as syndactylism, undescended testes and acrocyanosis.

REPORT OF A CASE

A. G., a single white woman aged 31, born in United States, a factory worker (fig. 2), had had a peculiar appearance of the face since birth; especially noticeable was the unusual position of her eyes. She was referred to the ophthalmologic clinic of the New York Hospital.
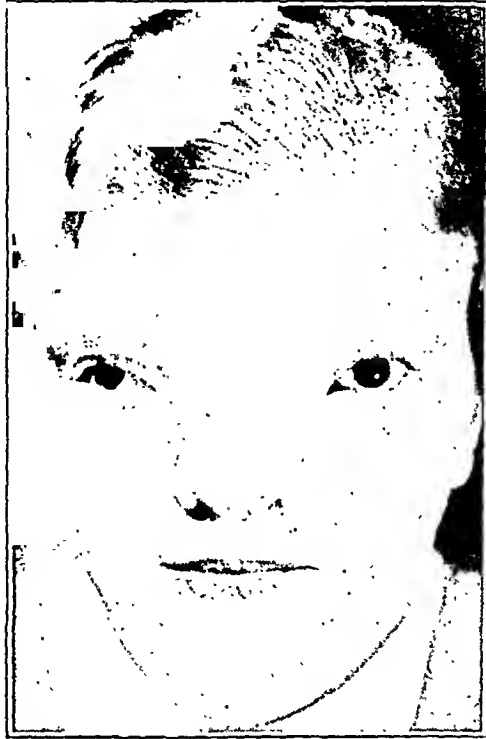
Fig. 2. — Appearance of the patient with hypertelorism.

The family history was essentially irrelevant. Inquiry regarding the other members of her family revealed nothing pertinent. There was no history of consanguinity among her forbears.

Her past history was essentially unimportant. Her general development was normal. Menstruation began at 17 and since had recurred regularly every twenty-seven days.

Her skull was wide, of the brachycephalic type. Its greatest circumference was 52.5 cm.; its greatest anteroposterior diameter, 17 cm., and its greatest width, 16 cm.

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10. (a) Gregory, H. H. C., and Bett, W. R.: Hypertelorism with Cleft Palate, Proc. Roy. Soc. Med. **26**:1016, 1933. (b) Whitwell, G. P. B.: A Case of Ectodermal Defect Associated with Hypertelorism, Brit. J. Dermat. **43**:648, 1931. (c) Reilly, W. A.: Hypertelorism: Report of Four Cases, J. A. M. A. **96**:1929 (June 6) 1931. (d) Allen, C.: Cephalic Dynostoses, J. Neurol. & Psychopath. **14**:332, 1934.

The frontal bosses were prominent, and the forehead between them was slightly depressed, especially toward the root of the nose.

The eyes gave the face a peculiar, animal-like appearance. They were far apart; this separation was further exaggerated by a right divergent squint, so that the eyes seemed to be looking in almost opposite directions. The palpebral fissures were slanted. The outer canthi were higher than the inner canthi, so that the eyes suggested mongolism. The distance between the inner canthi was 53 mm. and that between the outer canthi 110 mm.

The divergent squint of the right eye measured 140 prism diopters. This was checked by screening with prismatic correction and on the perimeter. Internal rotation of the right eye was limited. Otherwise, ocular motion of both eyes was normal.
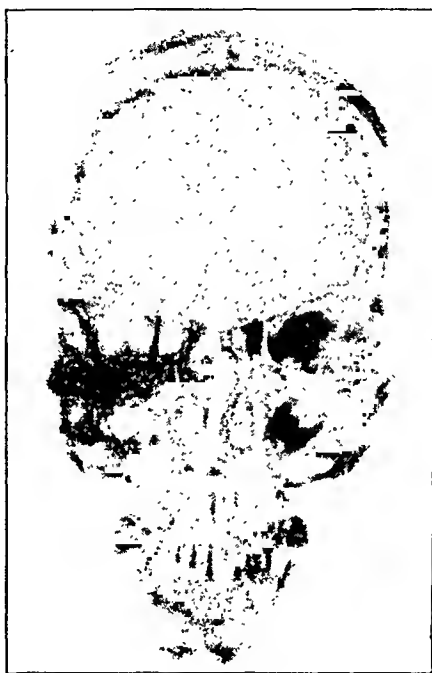
Fig. 3. — Roentgenogram of the skull of the patient with hypertelorism.

The interpupillary distance was 84 mm. The normal is usually close to 62 mm. Refraction under homatropine gave the following results:

Vision of 10/200 in the right eye with a + 4.00 D. sph.; vision of 20/20 in the left eye with a + 3.50 D. sph. + 0.50 D. cyl., axis 180.

The conjunctiva appeared normal, and the media were clear.

Examination of the right fundus disclosed pallor of the disk, attenuated retinal blood vessels and situs inversus. The macula appeared normal. The left fundus was normal in appearance.

The visual field of the right eye was concentrically contracted. With a 1 degree white test object it extended temporally 55 degrees, nasally 35 degrees, and downward 50 degrees. There was a relative central scotoma. The visual field of the left eye was normal.

The nose was heavy and wide. The root was flattened and the dorsum broad. The opening of the nares was large and quadrilateral. The mouth was normal.

The teeth were in good formation. There was a high arched palate. Physical examination otherwise gave negative results.

The patient appeared to be of normal intelligence.

The Wassermann reaction of the blood was negative. Urinalysis gave negative results.

Roentgen study of the head showed variation from the normal in a number of important features (fig. 3). The orbits were widely separated, corresponding to the large interocular distance previously described. The interorbital space was filled with ethmoid cells, which were increased in size and number. The inner edge of the orbit was a vertical straight line. Normally, this border is shorter and rounded. The sphenoid fissure was markedly enlarged and widened.

The optic foramens were small (fig. 4). The right was a horizontal oval, 2 by 4 mm. in size. The left was rounded, 3 mm. in diameter. The normal optic foramen is a vertical oval from 5 to 6 mm. in its longest diameter.[11] The small right optic foramen might well have been the cause for atrophy of the optic nerve and contraction of the visual field previously noted.

Fig. 4.—*A*, left optic foramen of the patient with hypertelorism. *B*, right optic foramen.

To improve the patient's appearance, operation for the squint was performed. The right internal rectus muscle was resected 5 mm. and the right external rectus muscle receded 5 mm. The conjunctiva was found to be exceedingly thin and friable. The internal rectus muscle was very frail, with few muscle fibers. The external rectus muscle was of the usual size.

ETIOLOGIC AND HEREDITARY FACTORS

The sphenoid bone has an important function of scaffolding the orbits. The lesser wings of the bone form the posterior part of the roof of each orbit. The anterior border is in contact with the orbital plate of the frontal bone. The processes of the lesser wings form the optic canals. Greig[7] expressed the belief that the disproportionately

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11. Whitnall, S. E.: The Anatomy of the Human Orbit, ed. 2, London, Oxford University Press, 1932, p. 28.

large size of the lesser wings formed the basis of hypertelorism. He theorized that in these cases the lesser wings ossified early in fetal life, about the third month, and laid the foundation for this anomaly.

Allen's [10d] theory is interesting. He expressed the belief that skull growth follows brain growth. The soft tissues ordinarily mold the bone. An artery or vein can form a groove in bone. Allen stated the opinion that the abnormal growth of part of the frontal lobes caused the skull to develop abnormally.

Most of the reported cases are isolated, with no familial incidence. A few family groups were reported by Cowan and Silberman,[12] and by Bojlén and Brems.[3] The trait appears to be a recessive characteristic.

TREATMENT

The only known prophylaxis is to advise patients with this condition not to propagate. Such patients present a limited opportunity for cosmetic surgical treatment. In our case some improvement was effected by an operation for squint. It is evident that with 140 prism diopters of divergent squint, only a slight improvement could be made. A nasal plastic surgical procedure was done by Pickerill,[13] with improvement noted in 2 cases.

OCULAR FINDINGS

The ocular findings are of special interest, but unfortunately they have not been reported in detail in the previous case reports. Squint was commonly noted. In those cases in which squint was not reported, no clear statement was made whether there was normal binocular vision. In some of the reports the illustrations show an obvious squint, though it is not mentioned in the text. It is our impression that squint occurs in almost all cases.

The cause of the squint is of interest. The wide interpupillary distance may be a factor. What distance limits the possibility of binocular vision? That can best be answered by more observations of these patients.

Also to be considered are local factors that may affect the eye. As stated before, in this anomaly the lesser wings of the sphenoid bone are enlarged. One must bear in mind that the lesser wings form the optic canals. Defects of the canal can affect the optic nerve which passes through it.

Our patient had narrowing and malformation of the optic canals. The constriction was more marked in the right canal. The right eye

12. Cowan, A., and Silberman, M.: Hypertelorism, J. Pediat. **3**:398, 1933.

13. Pickerill, H. P.: Hypertelorism: Notes on Three Cases, Brit. J. Surg. **26**:588, 1939.

showed a pallor of the disk, concentric contraction of the field of vision and a relative central scotoma. It seems likely that the narrowed optic canal was the cause of partial atrophy of the optic nerve.

At the operation in our case the internal rectus muscle was found to be very frail. All these points, either together or singly, may have caused the squint. The squint was in itself remarkable, a divergence of 140 prism diopters. We do not recall a case in which a greater divergence existed.

SUMMARY

Hypertelorism is a congenital anomaly of the skull and face characterized by wide separation of the orbits. The anomaly is believed to be due to an enlargement of the lesser wings of the sphenoid bone.

A case of hypertelorism is described. The interpupillary distance was 84 mm. There was a right divergent squint of 140 prism diopters. There was pallor of the right disk with concentric contraction of the visual field. Roentgenograms showed the anomalous arrangement of the orbits, narrowing and distortion of the optic canals.

CLINICAL STUDIES OF VITAMIN A DEFICIENCY

BIOPHOTOMETER AND ADAPTOMETER (HECHT) STUDIES ON NORMAL ADULTS AND ON PERSONS IN WHOM AN ATTEMPT WAS MADE TO PRODUCE VITAMIN A DEFICIENCY

BERTHA L. ISAACS, M.D.

FREDERIC T. JUNG, M.D., Ph.D.

AND

ANDREW C. IVY, M.D., Ph.D.

CHICAGO

The importance of an impaired nutritional state in relation to night blindness and other visual disturbances was recognized by the ancient Egyptians [1] as well as by Hippocrates.[2] Until 1934, when Jeans, Blanchard and Zentmire [3] reported the results of their studies among Iowa school children, night blindness was considered to occur rarely except during periods of religious fasting, famine or war.

If one is to accept the increasing number of reports in the literature, poor dark adaptation due to subclinical vitamin A deficiency occurs in approximately 40 to 50 per cent of the population.

Several excellent reviews [4] have appeared which discuss the theoretic as well as the practical aspects involved in the study of night blindness and dark adaptation. The clinical literature has been summarized by Jeghers [5] and by Sloan.[6]

1. Holcomb, R. C.: Night Blindness, J. A. M. A. **102**:786 (March 10) 1934.

2. Hippocrates: Oeuvres complètes, translated by E. Littré, Paris, J. B. Baillière, 1861, vol. 9, p. 159.

3. Jeans, R. C., and Zentmire, Z.: The Prevalence of Vitamin A Deficiency Among Iowa School Children, J. A. M. A. **106**:996-997 (March 21) 1936.

4. (a) Adams, D.: Dark Adaptation: A Review of the Literature, Medical Research Council, Special Report Series, no. 127, London, His Majesty's Stationery Office, 1929. (b) Hecht, S.: Rods, Cones and the Chemical Basis of Vision, Physiol. Rev. **17**:239-290 (April) 1937.

5. Jeghers, H.: (a) The Degree and Prevalence of Vitamin A Deficiency in Adults, J. A. M. A. **109**:756-761 (Sept. 4) 1937; (b) Review, Ann. Int. Med. **10**:1304-1334 (March) 1937.

6. Sloan, L. L.: (a) Instruments and Techniques for the Clinical Testing of Light Sense: I. Review of the Recent Literature, Arch. Ophth. **21**:913 (June) 1939; (b) II. Control of Fixation in the Dark-Adapted Eye, ibid. **22**:228-232 (Aug.) 1939; (c) III. An Apparatus for Studying Regional Differences in Light Sense, ibid. **22**:233-252 (Aug.) 1939.

The work of Tansley [7] and of Fridericia and Holm [8] stimulated further efforts to verify the relationship which they found to exist between the regeneration of visual purple, dark adaptation and night blindness. The chemical relationship between the light sensitive pigment, visual purple and vitamin A was clarified by Wald.[9]

Once this relationship was established, it became logical to seek visual methods for the detection of vitamin A deficiency. The methods [10] used have involved measurement of visual intensity discrimination or else the rate and final degree of dark adaptation.

The variety of instruments now available, as well as the divergent results reported, indicates that there is still considerable work to be done before photometric measurements can be relied on to detect subclinical vitamin A deficiency.

We have been interested in the detection and measurement of vitamin A deficiency for three years. When our work was started the biophotometer was the only clinical instrument available; later we were able to obtain one of the first Hecht adaptometers.[10e]

There are now only four reports [11] in the literature which critically analyzed and discussed the shortcomings of the biophotometer. Recently

7. Tansley, K.: The Regeneration of Visual Purple: Its Relation to Dark Adaptation and Night Blindness, J. Physiol. **71**:442-458 (April) 1931.

8. Fridericia, L. S., and Holm, E.: Experimental Contributions to the Study of the Relation Between Night Blindness and Malnutrition: Influence of Deficiency of Fat-Soluble A Vitamin in the Diet on the Visual Purple in the Eyes of Rats, Am. J. Physiol. **73**:79-84 (June) 1925.

9. Wald, G.: Carotenoids and the Visual Cycle, J. Gen. Physiol. **19**:351 (Nov.) 1935; Vitamin A in Eye Tissues, ibid. **18**:905 (July) 1935; Carotenoids and the Vitamin A Cycle in Vision, Nature, London, **134**:65 (July 14) 1934.

10. (a) Ferree, C. E., and Rand, G.: A New Type of Instrument for Testing the Light and Color Sense, Am. J. Ophth. **14**:325-333 (April) 1931. (b) Feldman, J. B.: Instrument for Determining Course of Dark Adaptation and for Measuring Minimum Light Threshold, Arch. Ophth. **12**:81-85 (July) 1934. (c) Jeans, P. C., and Zentmire, Z.: A Clinical Method for Determining Moderate Degrees of Vitamin A Deficiency, J. A. M. A. **102**:892-895 (March 24) 1934. (d) Edmund, C.: Some Methods of Testing Dark Vision, Acta ophth. **3**:153-169, 1926. (e) Hecht, S., and Shlaer, S.: An Adaptometer for Measuring Human Dark Adaptation, J. Optic. Soc. America **28**:269-275 (July) 1938. (f) Birch-Hirschfeld, A.: Ueber Nachtblindheit im Kriege, Arch. f. Ophth. **92**:18 (Dec.) 1916.

11. (a) Palmer, C. E., and Blumberg, H.: The Use of a Dark Adaptation Technique (Biophotometer) in the Measurement of Vitamin A Deficiency in Children, Pub. Health Rep. **52**:1403-1418 (Oct.) 1937. (b) Mutch, J. R., and Griffith, H. D.: A Study of Diet in Relation to Health: Dark Adaptation as an Index of Adequate Vitamin A Intake, Technique and Preliminary Results, Brit. M. J. **2**:565-570 (Sept. 18) 1937. (c) Isaacs, B. L.; Jung, F. T., and Ivy, A. C.: Vitamin A Deficiency and Dark Adaptation, J. A. M. A. **111**:777-780 (Aug. 27) 1938. (d) Steininger, G., and Roberts, L. J.: Biophotometer Test as Index of Nutritional Status for Vitamin A, Arch. Int. Med. **64**:1170 (Dec.) 1939.

Booher, Callison and Hewston [12] reported that they were able to detect only marked degrees of night blindness with this instrument in contrast to the mild deficiencies detected with the Hecht adaptometer.

Since the original clinical report [13] in which the adaptometer designed by Hecht was used, others have appeared.[14] We now present a summary of our results to date. These results pertain to: (1) an attempt to correlate the vitamin intake in the diet of medical students with biophotometer reading; (2) an attempt to produce a disturbance of vitamin A absorption and dark adaptation by giving relatively large doses of liquid petrolatum over a period of months to 28 students, using 29 others as controls; (3) an attempt to produce a disturbance of dark adaptation by a vitamin A deficient diet in 3 students, using the adaptometer designed by Hecht, and (4) the response of patients to vitamin A.

BIOPHOTOMETER

A description of the biophotometer and the technic of its operation has been reported so often that it seems unnecessary to repeat them. Those unfamiliar with the instrument are referred to the original article.[10c]

We have reported the details of our procedure elsewhere,[11c] but one point seems worth repetition. Immediately before the routine test was performed each subject sat in a room illuminated by a known constant light source. In a few instances some of the subjects were exposed for several minutes to bright sunlight immediately before entering the dark room for the test. Except for minor fluctuations, chiefly in the first reading, we were unable to detect any difference in effect on the photometer performance between preexposure to normal or excessively bright light. Booher, Callison and Hewston [12] were unable to detect significantly altered requirements for vitamin A when there was either a marked increase or decrease in exposure of the eyes of normal adults to an ordinary light source. The observation by Aykroyd [15] that Alaskan fishermen habitually blindfold one eye and later expose it and blindfold the other as a cure for their night blindness makes the factor of illumination prior to a test of interest.

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12. Booher, L. E.; Callison, E. C., and Hewston, E. M.: An Experimental Determination of the Minimum Vitamin A Requirements of Normal Adults, J. Nutrition **17**:317-331 (April) 1939.

13. Haig, C.; Hecht, S., and Patek, A. J., Jr.: Vitamin A and Rod-Cone Dark Adaptation in Cirrhosis of the Liver, Science **87**:534-536 (June 10) 1938.

14. Booher, Callison and Hewston.[12] Booher and Callison.[18] Wald, Jeghers and Arminio.[29] Steffens, Blair and Sheard.[32] Pett.[33]

· 15. Aykroyd, W. R.: Night Blindness Due to Vitamin Deficiency, Tr. Ophth. Soc. U. Kingdom **50**:230-233, 1930.

Method of Study.—One hundred and forty-three healthy medical students cooperated in this study. In order to determine the day-to-day variation in a single subject's photometer readings, as well as the variations to be found between different persons, 20 of the subjects were chosen for intensive study. There were 16 males and 4 females in the group, with an age range between 20 and 45 years. A single observer tested each of the 20 subjects daily at the same hour for ten consecutive days. Inquiry and study of the diet revealed that every subject was ingesting a well balanced diet which was adequate in all the essential factors; in addition, no one had either a chronic illness or a recent severe one.

Because it had been suggested by Jeans and Zentmire [10c] that fatigue might influence dark adaptability in an adverse manner, we retested a number of our subjects at the end of a long arduous day. No significant changes from the usual daily readings were obtained.

Analysis of the performances on the biophotometer of these 20 students, in addition to that of the 123 subsequently tested, showed that the results frequently varied widely from day to day; also that a subject might appear deficient one day and normal on all ensuing days. This was on the basis of the criteria proposed by Jeans. However, our previous report [11c] indicated the unreliability of certain of the biophotometer readings and referred to the criteria which we used for an evaluation of results.

The remaining 123 medical students were tested twice, one week apart at the same hour of the day. Their ages ranged from 19 to 34; all were apparently healthy.

Relationship of Diet to Biophotometer Performance.—We were primarily interested in finding a correlation between biophotometer performance and dietary vitamin A intake; hence detailed records of the types and approximate quantities of all food consumed for both five and seven day periods were kept by each subject. Vitamin A values of the diets were then ascertained from the tables of Daniel and Munsell.[16] We chose the lowest values listed for each food; therefore, final values represent the minimal rather than the most probable intake.

The calculated vitamin A intake was found to range between 950 and 9,725 U. S. P. (international) units per day. The mode for our group was 3,001 to 4,000, which is about the same as for the combined groups of normal and subnormal medical students tested with the biophotometer by Jeghers.[5a] Three thousand U. S. P. (international) units

16. Daniel, E. P., and Munsell, H. E.: Vitamin A Content of Foods, Miscellaneous Publication 275, United States Department of Agriculture, 1937.

of vitamin A daily have been recommended [17] as essential for the maintenance of normal storage in the adult. In her last report Booher [18] indicated that slightly more than this quantity, i. e., 47 to 57 units of vitamin A per kilogram of body weight, was necessary for the maintenance of a normal dark adaptation in normal adults when the vitamin A value of the diet was derived almost entirely from the carotene in cooked green peas. A still higher intake was required when the vitamin A source was from the carotene in cooked spinach.

Edmund and Clemmesen [19] found that young adult males on prison fare showed seasonal oscillations in visual distinctive power when their average vitamin A intake from diet was 1,250 international (U. S. P.) units daily. When this intake was elevated to 1,400 units daily by the addition of milk to the dietary, visual distinction powers remained normal at all times.

Between 70 and 85 per cent of our subjects took more than 3,000 U. S. P. units daily; another 15 to 30 per cent ingested between 1,000 and 3,000 units daily. Ingestion of the latter amounts might result in night blindness if the intake was low over a long enough period. A bare 1 per cent of our subjects took slightly less than 1,000 units daily.

These values appear to be significant, for there was but 1 student of the 143 who showed signs of subnormal dark adaptation. This student was otherwise clinically normal; his dietary vitamin A intake was calculated at 10,000 units daily; ophthalmologic examination revealed no abnormalities; still his biophotometer performances on numerous occasions indicated the worst possible threshold for dark adaptation. The wide fluctuations which occurred in his readings were attributed to the lack of a fixation point in the apparatus used for testing. Administration of oleum percomorphum [20] and carotene [21] in doses to furnish approximately 50,000 U. S. P. (international) units of vitamin A daily failed to effect consistent improvement in his biophotometer readings.

Each subject under observation was asked to give information in regard to the following matters: number and duration of infections of the upper respiratory tract; headaches; condition of skin; eye fatigue;

17. Booher, L. E.: Vitamin A Requirements and Practical Recommendations for Vitamin A Intake, J. A. M. A. **110**:1920-1925 (June 4) 1938.

18. Booher, L. E., and Callison, E. C.: The Minimum Vitamin A Requirement of Normal Adults: II. The Utilization of Carotene as Affected by Certain Dietary Factors and Variations in Light Exposure, J. Nutrition **18**:459-471 (Nov. 10) 1939.

19. Edmund, C., and Clemmesen, S.: On Parenteral A Vitamin Treatment of Dysaptatio (Nyctalo-Hemeralopia) in Some Pregnant Women, Acta med. Scandinav. **89**:69-92, 1936.

20. Supplied by Mead Johnson & Company, Evansville, Ind.

21. Supplied by the S. M. A. Corporation, Cleveland.

irritation of eyes as indicated by inflammation or burning; ability to see in darkened theaters or on the streets at night; gastrointestinal habits in regard to dyspepsia, pain, appetite changes and bowel habits; urinary habits, and changes in weight.

Individual answers were analyzed in relation to the subjects' vitamin A intake, general diet and biophotometer performance. Various forms of statistical analyses were utilized, but none of them indicated any significant correlation. In fact, many whose vitamin A intake was at a high level reported the presence of some symptoms generally attributed to A deficiency; the reverse was also true. In spite of the fact that the questionnaire was largely of a subjective nature, we believe that any trends toward correlation would have been easily detected.

BIOPHOTOMETER PERFORMANCE IN ATTEMPTED VITAMIN A DEFICIENCY

For the detection of night blindness, Jeans and Zentmire [10c] attributed importance to the readings obtained immediately after exposure to the bright light of the biophotometer as well as to the one obtained ten minutes later. Although we had evidence to prove that these were not the most statistically reliable readings, we utilized them to pick out "normal" and "subnormal" persons for further study.

From the results with the 123 subjects, we obtained the median for readings 4 and 7 and selected the group for further study as follows: Twenty-five with readings nearest the median and 11 with readings farthest below the median were chosen from the results of reading 4; 25 with readings nearest the median and 5 with those farthest below the median were selected on the basis of reading 7. Those with readings nearest the median were considered normal; those with readings farthest below it were considered subnormal. This division provided us with 66 subjects, 50 of whom were normal and 16 subnormal. By alternate selection, 21 normal and 8 subnormal subjects were allotted to groups A and C respectively. These were the control, or nontreated, groups. The remaining 20 normal and 8 subnormal subjects were designated as groups B and D. The latter were given a highly emulsified form of liquid petrolatum [22] in doses which provided approximately 5 cc. of oil per kilogram of body weight. The oil was taken nightly before retiring.

Biophotometer performance was determined for each subject biweekly for between three and four months. Any unusual symptoms were reported to us. The nature of the medication was unknown to the subjects, and efforts were made to disguise the uniformity of medication by marking successive bottles in different ways.

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22. Sixty-five per cent emulsified solution of liquid petrolatum, agar and water.

In order to evaluate further the results obtained from photometric readings, we formulated two indexes which are designated as index B and index C. Index B is the sum of biophotometer dial readings 2, 3, 5 and 6 obtained in a single test. Index C is $1/2$ $(B_1 + B_2)$; B_1 represents the index of the first photometer test and B_2 the second test. Index C was then taken to be the subject's "basal" reading, and all subsequent readings were evaluated by subtracting that day's index B from his index C. This provided us with a value above or below the basal. After the persons in each group had been followed for from ninety-one to one hundred and thirty-one days, the groups were again subdivided by alternate selection of subjects. The scheme below indicates the origin and number of the subjects in each division:

Original Distribution	Regimen	Final Distribution and Regimen
Group A—21 normal subjects	No medication	11 given vitamin A
Group C— 8 subnormal subjects	prior to vitamin A	12 given no vitamin A
Group B—20 normal subjects	liquid	13 continued on liquid petrolatum plus vitamin A
Group D— 8 subnormal subjects	petrolatum daily	12 continued on liquid petrolatum alone

The results for the 29 subjects (21 normal and 8 subnormal) were compared with those of the 28 (20 normal and 8 subnormal) subjects who took liquid petrolatum daily for the same period of time. The biophotometer performances of the 12 persons who received 200,000 units of vitamin A [23] daily for fourteen days in addition to their daily dosage with oil were compared with the performances of 11 subjects who had not taken oil but who received identical supplements of vitamin A.

In a like manner the biophotometer performances of the 12 subjects who took oil daily without supplements of vitamin A were compared with the performances of the 13 subjects who received 200,000 units of vitamin A daily for fourteen days in addition to their daily oil.

Table 1 indicates the clinical signs and symptoms which were recorded by the subjects while taking the liquid petrolatum.

The results from the questionnaire as well as direct observation of the subject indicate that no clinically evident deviations from the normal occurred at any time during the experiment. This was to be expected from the results of animal experiments in which similar quantities of liquid petrolatum have been shown to exert no appreciable influence on

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23. This was a special fish liver oil blend supplied by Dr. Carl Nielsen, director of nutritional research, Abbott Laboratories; 200,000 units of vitamin A and 2,700 units of vitamin D were provided in the daily dose of 56 drops.

utilization of vitamin A.[24] Its harmful influence on the utilization of carotene has been demonstrated in animals and recently by clinical studies.[25] Against the production of distinct vitamin A deficiency by ingestion of large doses of liquid petrolatum was the fact that our subjects consumed relatively high vitamin A diets, and so far as could be determined they lacked all organic conditions which might interfere with the absorption and utilization of the vitamin. It is of interest here to record the fact that 3 of our subjects who were found to have readily evident chronic hemolytic jaundice had repeatedly normal responses to biophotometer tests.

TABLE 1.—*Signs and Symptoms Recorded by Normal Subjects Who Took Liquid Petrolatum Daily* *

Sign or Symptom	Number Reporting	Results
Frequent colds......................	24	6 had increased number
Condition of skin..................	24	7 had increased oiliness
Change in present acne...........	13	2 became worse; 4 improved; 7 remained unchanged
Eyes:		
Ability to use eyes for study..	24	No change
Redness.......................	24	No change
Burning.......................	24	No change
Ability to see in dark..........	24	No change
Gastrointestinal symptoms:		
Colicky abdominal pains......	24	12 had pains during 1st week only; those of 1 continued into 2d week
Abdominal flatus..............	24	12 had flatus during 1st week; only 6 had this symptom during 2d week
Flatus per anum...............	24	22 had this symptom during 1st week and 15 during 2d week
Borborygmi...................	24	15 had this symptom during 1st week and 10 during 2d week
Nausea.......................	24	8 were nauseated during 1st week and 2 during 2d week
Appetite......................	24	Unchanged
Fulness after eating..........	24	2 had this symptom during 1st week and none during 2d week
Leakage of oil................	24	17 had leakage of oil during 1st week and 8 during 2d week
Number of stools.............	24	20 reported average increase of 4.2 stools per week during daily medication †
Strength of urge..............	24	Unchanged
Ease of passage.	24	Unchanged

* The amount of oil taken was 5 cc. per kilogram of body weight.
† Seventeen of 24 reported an average decrease of 4.1 stools per week during seven days immediately following withdrawal of oil.

24. (*a*) Rowntree, J. I.: The Effect of the Use of Mineral Oil upon the Absorption of Vitamin A, J. Nutrition **3**:345-351 (Jan.) 1931. (*b*) Dutcher, R. A.; Harris, P. L.; Hartzler, E. R., and Guerrant, N. B.: Vitamin Studies: The Assimilation of Carotene and Vitamin A in the Presence of Mineral Oils, ibid. **8**:269-283 (Sept.) 1934. (*c*) Jackson, R. W.: The Effect of Mineral Oil Administration upon the Nutritional Economy of Fat-Soluble Vitamins: I. Studies with Vitamin A of Butter Fat, ibid. **4**:171-184 (July) 1931; II. Studies with Vitamin A Factor of Yellow Corn, ibid. **7**:607-616 (June) 1934; III. Studies with Vitamin D of Irradiated Ergosterol, ibid. **7**:617-622 (June) 1934. (*d*) Mitchell, H. S.: Influence of Mineral Oil on Assimilation of Vitamin A from Spinach, Proc. Soc. Exper. Biol. & Med. **31**:231-233 (Nov.) 1933.

25. Curtis, A. C., and Kline, E. M.: Influence of Liquid Petrolatum on Blood Content of Carotene in Human Beings, Arch. Int. Med. **63**:54-63 (Jan.) 1939.

The liquid petrolatum was taken two hours after the last meal. This allowed time for the absorption of nutrient material from the intestine and precluded the possibility of having the vitamin A washed out of the intestinal canal quantitatively by the oil, as has been shown to occur when carotene and oil are given.[25] When the supplement of vitamin A was added, it was administered with the meals so as to insure maximum absorptive possibilities.

It is to be noted that we employed unusually large doses of vitamin A (200,000 units daily). It has been shown that the rat utilizes vitamin A most efficiently when his intake is near his minimum requirements and also that his efficiency decreases as the amounts provided become in excess of his needs.[26] Such results have not been demonstrated for the human subject, and since our clinical observation on patients on a deficient diet indicated the need for massive therapeutic doses rather than the smaller ones generally administered, we elected to give the doses described.
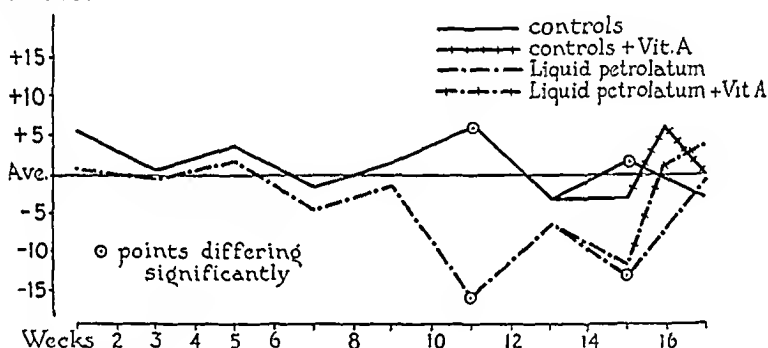
Chart 1.—Dark adaptation (plotted as deviations from the average) as affected by the taking of liquid petrolatum. The biophotometer scores of 29 subjects who took liquid petrolatum are contrasted with the scores of 24 subjects who took none. After thirteen weeks, half of each group received vitamin A. The results do not show any consistent effects of either the liquid petrolatum or the vitamin. (Numerical data are presented in table 2.)

Inspection of chart 1 gives the impression that at about the ninth week of administration of liquid petrolatum the biophotometer performance (as judged from the average index B for the group) was markedly reduced. This apparent effect continued with minor fluctuations up to the fifteenth week, when there was a sharp unexplainable rise toward the base line. Were it not for this last rise, the seeming effect of ingestion of vitamin A on the subjects fed liquid petrolatum would have been beneficial. The relative constancy of index B in the

26. Baumann, C. A.; Riising, B. M., and Steenbock, H.: Fat-Soluble Vitamins: The Absorption and Storage of Vitamin A in the Rat, J. Biol. Chem. 107:705-715 (Dec.) 1934.

nonmedicated group of controls, even after one half of them were given vitamin A, also inclines one to accept the validity of the data.

However, statistical analysis of our data tends to nullify the visual impression of both the adverse effect of liquid petrolatum on biophotometer readings and the improvement under vitamin A therapy. It is evident from table 2 that the only results which approach statistical significance according to Fisher's rule are the values obtained during the tenth to twelfth weeks and the fourteenth to the sixteenth weeks. These

TABLE 2.—*Summary of the Deviations and Probable Error of the Deviations of Index B from Index C for the Groups Indicated* *

	Control Group (No Medication)				Group Receiving Liquid Petrolatum Medication Daily		
Week of Experiment	Number in Group	Deviation from Original Level (Index C- Index B)	Probable Error of Deviation	Week of Experiment	Number in Group	Deviation from Original Level (Index C- Index B)	Probable Error of Deviation
0- 2	24	+5.79	±2.07	0- 2	29	+0.09	±2.06
2- 4	24	+0.33	±1.91	2- 4	28	—0.69	±1.60
4- 6	18	+3.39	±2.66	4- 6	27	+1.41	±2.62
6- 8	15	—1.40	±2.26	6- 8	24	—4.33	±2.66
8-10	14	+1.43	±3.37	8-10	25	—1.52	±3.08
10-12	15	+6.20 †	±2.68	10-12	17	—16.47 †	±3.03
12-14	20 ·	—3.25	±3.03	12-14	23	—6.56	±2.50
14-16	17	+1.77 †	±3.24	14-16	28	—13.25 †	±2.95
16-18	13	—3.23	±4.28	16-18	14	—1.36	±4.34

Part of Group Given 200,000 Units Vitamin A				Part of Group Given 200,000 Units Vitamin A Daily Plus Liquid Petrolatum			
Days on Vitamin A				Days on Vitamin A			
1- 5	8	—3.10	±3.85	1- 5	11	—11.54	±6.29
6-10	6	+6.00	±3.95	6-10	10	+0.80	±4.90
11-15	8	—0.37	±6.70	11-15	10	+4.10	±4.20

* See chart 1.
† The results are statistically significant. Only the two pairs of figures marked by the dagger differ significantly according to Fisher's rule.

points are encircled on chart 1. None of the differences obtained during administration of vitamin A are statistically significant.

Our conclusions from this part of the experimental study must be that straight graphing of values suggests that the prolonged administration of liquid petrolatum reduces the subject's ability to become adapted to dark and that the ingestion of large doses of vitamin A concentrate tends to improve their dark adaptation. On the basis of statistical analysis, however, the final conclusions must be that unexplainable fluctuations governed by forces of which we have no knowledge do occur. Because the majority of these fluctuations are not mathematically significant, the results from this study must be considered inconclusive. One must bear in mind that the apparatus used to obtain the foregoing results

was, according to observations published elsewhere by us, inadequate for quantitative studies and, second, that the factors responsible for part of the fluctuation shown in table 1 and chart 1 might have been the seasonal factor which Blegvad [27] studied so extensively.

ADAPTOMETER

According to Hecht,[4b] there are at least six specifications which must be met before precise quantitative measurements of dark adaptation may be made. These requirements he incorporated in an apparatus which we were able to obtain for this study.

Method of Study.—Preliminary observations indicated that accurate and consistent readings could be obtained by us when normal subjects were tested with this adaptometer. In order to eliminate any variations
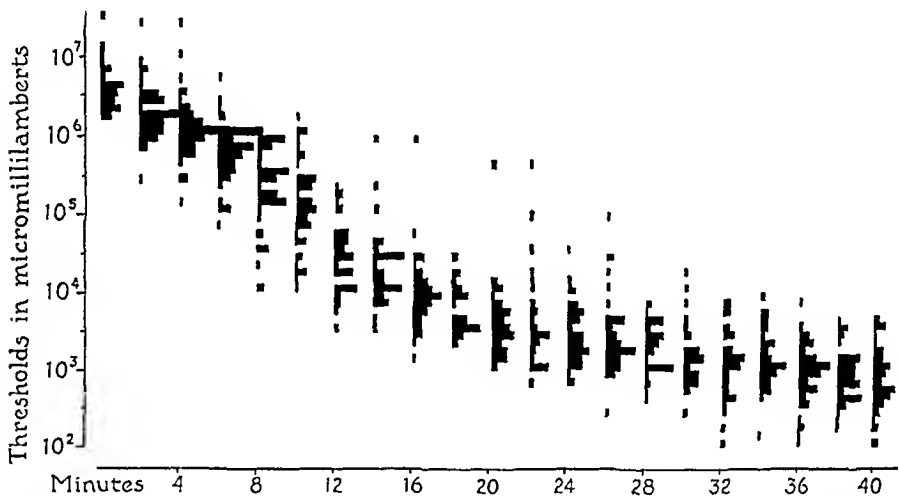
Chart 2.—Composite adaptometer data of 68 normal subjects. As the subject sits in total darkness, the progress of his dark adaptation from minute to minute is measured by the brightness of the dimmest light he is able to perceive.

introduced by the operator, all our early tests were conducted by a single operator; later tests were made interchangeably by two of us. Sixty-eight apparently healthy normal persons, taking adequate diets, were tested one or more times. The ages ranged between 20 and 50, and the group included males and females. Although age has been shown to cause a slight increase in cone threshold, it does not seem to effect any change in the rod threshold. Most observers have attributed this effect to changes in the ocular media themselves, but this conclusion appears to be inadequate to explain the entire phenomenon. Hecht

27. Blegvad, O.: Xerophthalmia, Keratomalacia and Xerosis Conjunctivae, Am. J. Ophth. **7**:89-117 (Feb.) 1924.

and Mandelbaum [28] concluded, after studying over 100 normal persons, that sex had no influence on the final rod or cone thresholds nor on the cone-rod transition time.

The maximum day-to-day variation in threshold intensity as measured by the adaptometer was found by Hecht and Mandelbaum [28] not to exceed 0.3 log unit. Between different persons they found a range no greater than 1.0 log unit. Wald, Jeghers and Arminio [29] found the maximum day-to-day variations for the rod threshold to be 0.2 log unit.

The final rod thresholds of different subjects in our normal group of 68 subjects likewise showed a range no greater than 1.0 log unit. However, in this group of normal subjects we found persons whose daily fluctuations varied between 0.4 and 0.6 log unit.

The cone-rod transition time for our normal subjects ranged within the six to ten minute period noted by Hecht and others; however, the transition time for some of our subjects varied by as much as two to three minutes when they were tested on different days.

VITAMIN A DEFICIENCY AND THE ADAPTOMETER (HECHT)

Experimental Vitamin A Deficiency.—Three apparently healthy normal medical students volunteered to live on a vitamin A–deficient diet in order that measurements of their dark thresholds could be followed throughout the depletion period as well as during a period when the diet was supplemented with vitamin A. The experiment was begun in September and ended in December 1938.

Through the cooperation of Miss Edith Graham and Miss Elizabeth Runkel, dietitians at the Passavant Memorial Hospital, arrangements were made to serve all meals from the hospital kitchen. The maximum values given in the tables by Daniel and Munsell were used to ascertain the daily vitamin A content of the diet. In addition, each subject received 15 grains (0.97 Gm.) of calcium lactate three times a day; 50 mg. of ascorbic acid [30] daily and large doses of a concentrate which furnished adequate amounts of the entire vitamin B complex. This contained no vitamin A and yielded 2,400 units of B_1 daily. Care was taken to provide a diet which was adequate not only in all other essentials but which was also attractive and palatable. At first the lack of usual color in the diet was a disturbing factor, but as the regimen progressed the dietitians were able to provide enough variety to satisfy all demands.

28. Hecht, S., and Mandelbaum, J.: Rod-Cone Dark Adaptation and Vitamin A, Science **88**:219-221 (Sept. 2) 1938.

29. Wald, G.; Jeghers, H., and Arminio, J.: An Experiment in Human Dietary Night Blindness, Am. J. Physiol. **123**:732-746 (Sept.) 1938.

30. Supplied by Merck and Company, Rahway, N. J.

It was possible to maintain an average daily intake of less than 74 units of vitamin A. In previous studies with normal medical students we had found the usual average daily intake of vitamin A to be above 5,500 units.

In addition to dietary control, urinalyses and complete blood counts were obtained at suitable intervals throughout the depletion period. Daily records of weight which were kept showed no marked changes except for subject G., whose weight was greatest. He showed a total loss of weight of about 8 pounds (3.6 Kg.) at the end of the depletion period. This student was carrying an unusually heavy class schedule during the experiment, with consequent loss of sleep; hence one must be cautious in attributing the decrease in weight to the depleted diet alone.

The generous cooperation of Dr. Helen Holt, of the department of ophthalmology, enabled us to obtain frequent records of the 3 subjects' visual acuity as tested with the Snellen and Jaeger test charts. Peripheral fields were examined with the Ferree-Rand perimeter, a 3 mm. white target being used. Central fields were tested on the tangent screen, a 2 mm. and a 1 mm. white test object being used at a distance of 1 meter. Tests were made before starting the diet, again on the seventeenth, twenty-fourth, thirty-fourth and forty-third days of the deficiency period. These were repeated one hour after the first dose of vitamin A concentrate was given, and on the ninth, twenty-first, twenty-eighth, thirty-fifth and forty-second days thereafter.

Experience with 2 night-blind patients [31] who were known to have been on vitamin A–deficient diets for some time suggested that contraction of the visual fields accompanied vitamin A deficiency and that a return to normal fields was rapid under vitamin A therapy. For this reason we hoped to obtain interesting data by following the vision and fields during the course of vitamin A depletion in our 3 subjects.

Campimeter Results.—At times our subjects showed contractions of the visual fields which were almost as great as that recorded by Sloan,[6c] but these changes were erratic, and we felt that they could well be accounted for on the basis of the apparently physiologic variations which are frequently obtained among normal persons. There were periods when we felt that the nervous apprehension over the appearance of vitamin deficiency contributed considerably to the fluctuations in the fields of 1 of our subjects.

SUBJECT S.—The visual fields exhibited erratic changes in configuration which gave the impression of progressive shrinkage of the fields. Actual measurements of the area of the fields with a planimeter revealed no consistent decrease, as on some days the fields would be larger or smaller without any apparent relation to

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31. Provided by Dr. Sanford Gifford.

sight or symptoms. The measurements of the blindspot also fluctuated. Vision remained practically unchanged for the two eyes, ranging between 20/10 to 20/15 for the right eye and 20/25 — 2 to 20/65 + 2 for the left eye.

SUBJECT G.—The visual fields were somewhat contracted on the sixteenth, thirtieth and thirty-seventh days but were again apparently normal on the forty-fourth day. The sixteenth day was the period at which the subject complained of blurred vision in bright light; the thirtieth day was during the time when the nails were cracked; no symptoms were present on the thirty-seventh day. The blindspot was of almost constant size throughout. Vision in the right eye was constant at 20/13; vision in the left eye ranged between 20/13 and 20/15 — 1.

SUBJECT L.—The peripheral fields assumed bizarre forms at frequent intervals throughout the experiment, but at no time was there evidence of actual diminution in size. The size of the blindspot varied inconsistently but was definitely larger
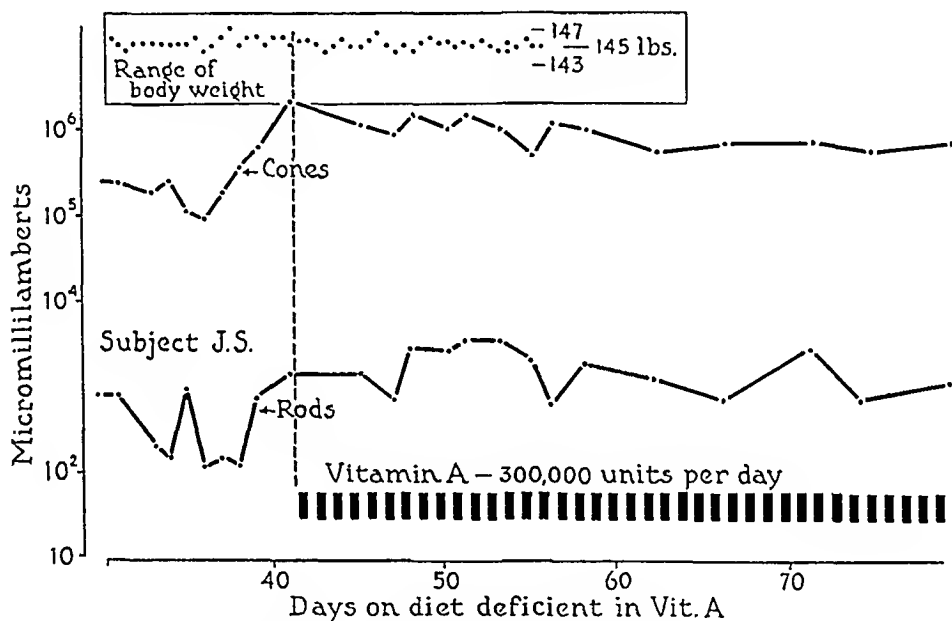
Chart 3.—Effects of suddenly increasing the intake of vitamin A. Daily doses of 300,000 units of vitamin A affected neither the weight nor the adaptometer score of J. S., whose vitamin A intake had averaged less than 74 units per day for forty-one days.

one month after cessation of the diet (vitamin A concentrate was continued during the entire month) than at any time during the depletion period. Vision in the right eye varied from 20/15 — 2 to 20/25 and in the left eye from 20/25 to 20/15 + 2.

These results reveal a lack of consistent differences either in the visual fields of the subject or between different subjects.

Adaptometer Results.—Contrary to the results of Wald, Jeghers and Arminio [29] as well as of Hecht and Mandelbaum,[28] none of our subjects showed either clinical or photometric evidence of vitamin A deficiency during the early days of vitamin A deprivation. Our results
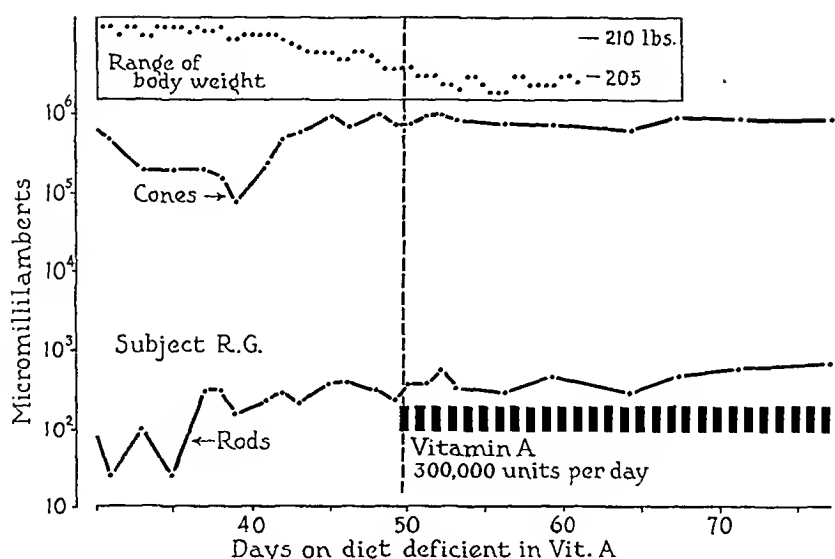
Chart 4.—Effects of suddenly increasing the intake of vitamin A. R. G. was initially somewhat overweight. During forty-nine days on a diet deficient in vitamin A, his weight declined toward the normal. Suddenly raising his vitamin A intake to more than 300,000 units per day affected neither his weight nor his adaptometer performance.
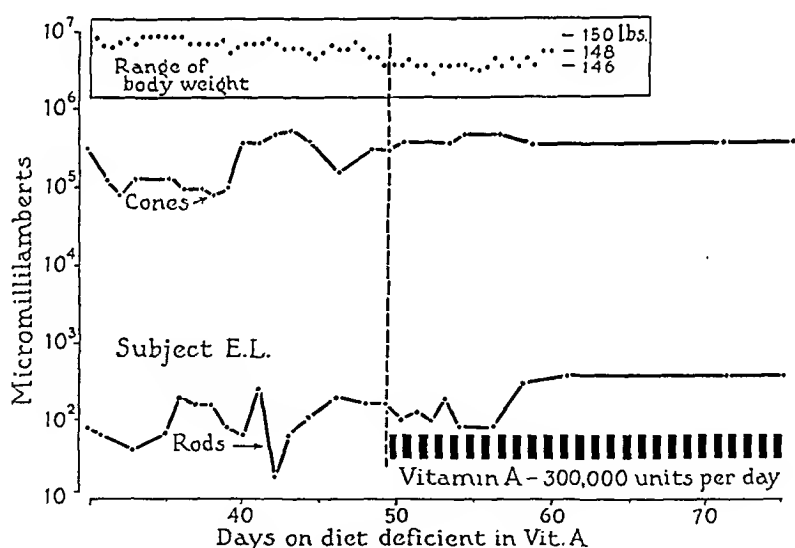
Chart 5.—Effects of suddenly increasing the intake of vitamin A. No convincing effects were seen in either the weight or the adaptometer performance of subject E. L. when his intake of vitamin A was suddenly raised from *less* than 74 to more than 300,000 units per day.

more nearly duplicated those recently reported by Booher and Callison [18] and by Steffens, Blair and Sheard.[32] One of our subjects (G) indicated blurring of vision (table 3) on the fourteenth to seventeeth days with some suggestion of night blindness on the twentieth day of the diet, but it

TABLE 3.—*Clinical Symptoms of Three Experimental Subjects Maintained on a Vitamin A Deficient Diet* *

Day of Regimen	Clinical Symptoms
Subject G	
Normal	Urine: Normal
	Blood: Hemoglobin, 15.48 Gm.; red cells, 5,430,000; white cells, 8,250
14	Blurred vision in bright light
17	Vision still blurred; lights appeared yellow; able to see well in darkened theater
20	Haze over everything, especially at night; rhinitis for 4 days
24	Urine: Normal
	Blood: Hemoglobin, 14.12 Gm.; red cells, 5,000,000; white cells, 5,150
25	Mucoid nasal discharge continued
27-30	Cracking of nail beds
33	Eyes very dry in morning
42-44	Constant headache
45-47	Nosebleed; definite night blindness; urine, normal
46	Ulcer on right nasal septum
49	Administration of 300,000 units of vitamin A started; diet the same
5 days after administration of vitamin A	Photophobia and blurring of lights at a meeting when bright lights were turned on
38 days after administration of vitamin A	Blood: Hemoglobin, 15.48 Gm.; red cells, 5,150,000; white cells, 5,700
Subject S	
Normal	Urine: Normal
	Blood: Hemoglobin, 16.32 Gm.; red cells, 5,470,000; white cells, 6,100
5	Inconsistent readings on photometer
11	Extremely inconsistent readings on photometer
18	Rhinitis; headache; raw throat for 2 days; flatulence; loose stools
	Urine: Normal
	Blood: Hemoglobin, 15.04 Gm.; red cells, 6,001,000; white cells, 10,500
20	Nasopharyngitis persists; stools normal
30	Nausea; loose stools
31	Eyes dry; conjunctivas dull; scrapings negative
33	Eyes extremely dry, especially in morning
39	Night blindness; eyes no longer dry; no gastrointestinal symptoms
42	Raw throat; eyes very dry
43	Urine: Normal
	Blood: Hemoglobin, 13.93 Gm.; red cells, 4,520,000; white cells, 5,950
	Administration of 300,000 units of vitamin A started; diet the same

* Subject L had no signs or symptoms of any variation from the normal. The urine was always negative, and the blood picture was unchanged from the normal.

was not until the thirty-seventh day that any suggestion of a definite increase in final rod threshold appeared. On the forty-fifth day there was some increase in the cone threshold. Subject S began to have

32. Steffens, L. F.; Blair, H. L., and Sheard, C.: Photometric Measurements on Visual Adaptation in Normal Adults on Diets Deficient in Vitamin A, Proc. Staff Meet., Mayo Clin. **14**:698-704 (Nov. 1) 1939.

clinical complaints on the eighteenth day of the diet with a slight increase in final rod threshold on the thirtieth day and a definite increase in cone threshold on the forty-first day. Curiously, his cone and rod threshold remained apparently elevated throughout the period of normal diet plus vitamin A supplements. Subject L never reported any symptoms which by a far stretch of imagination could be attributed to the change in his dietary regimen.

The results may be summarized by stating that at no time during the forty-three or forty-nine days on the deficiency diet did any of our subjects show clearcut evidence of impaired dark adaptation. It can be noted, however, that throughout the depletion period there was a general trend, in addition to occasional sizable fluctuations due to unknown variables, toward a higher threshold, i. e., slight impairment of dark adaptation. It is significant that the average for 25 normal persons studied during the same period (October-November) showed a similar drift. This drift may well be a seasonal fluctuation associated with the dietary and metabolic variation attendant on changed climatic conditions. Such a seasonal fluctuation has been extensively studied in cattle and in the human subject.[27] Recently, Pett[33] found considerable shift in the results of photometer readings obtained when his 500 Canadian subjects were tested in October and again in January. Of those subjects who had normal dark adaptation in October, 26 per cent were the same in January; 26 per cent showed slight deficiency in January and 48 per cent more were definitely deficient by the same period. Among those deficient in October, 21 per cent were normal by January (chiefly after treatment), 24 per cent remained the same and 55 per cent were more deficient. Whether these changes are actually due to seasonal factors remains to be decided by more extensively controlled experiments.

Pett is the only recent writer who has recorded his clinical observations along with the photometric measurements. In himself, while on a deficient diet he observed signs possibly related to the diet poor in vitamin A. We interviewed our subjects daily during the entire regimen for the appearance of any significant signs or symptoms. The significant findings are recorded in table 3. It is of interest that L, who had the most phlegmatic temperament of the 3 subjects, reported no symptoms other than frequent exacerbations of a chronic sinusitis. These he did not think were of any greater frequency than in previous years.

None of our 3 subjects showed any consistent change in the cone-rod transition time while on a deficient diet. In their study of patients with cirrhosis of the liver, Haig, Hecht and Patek[13] noted a delayed cone-rod transition time which tended to decrease during treatment

33. Pett, L. B.: Vitamin A Deficiency: Its Prevalence and Importance as Shown by a New Test, J. Lab. & Clin. Med. 25:149-160 (Nov.) 1939.

with vitamin A. This tendency did not appear in their group rendered hypovitaminotic by diet alone.

Response to Vitamin A Therapy.—On the forty-third day of the deficient diet, subject S received the first of a series of daily doses of a vitamin A concentrate.[34] The 56 drops given provided approximately 300,000 U. S. P. units of vitamin A and 2,700 units of vitamin D. Subjects G and L each received the same supplements, starting on the forty-ninth day. Except for minor, apparently insignificant fluctuations, their final thresholds showed no actual improvement incident to the ingestion of these extraordinarily large doses of vitamin A. On the fifty-fourth day the subjects discontinued the hospital regimen and returned to their customary habits of eating. The vitamin A supplements were continued largely as a safety measure to insure adequate available sources of the vitamin for the replacement of probably low storage. Each subject was occasionally retested several months after the experiment was entirely discontinued, but no real differences in the thresholds as compared with previous readings could be detected. At no time during the experiment did any of the thresholds come within even 1.5 log units of the thresholds of persons whose night blindness was the result of organic retinal changes.

OBSERVATIONS ON CLINICAL PATIENTS NOT ON AN EXPERIMENTAL REGIMEN

PATIENT 1.—J. G., a broker aged 57, complained of difficulty in seeing at night or in a dark room, of marked glare from headlights at night and of frequent headaches.

Ophthalmologic examination was made by Dr. Helen Holt. External examination revealed no abnormalities; examination with the slit lamp and the ophthalmoscope showed the fundi and fields to be normal. Vision without glasses was 20/200 in the right eye and 20/200 in the left eye. With glasses, vision was 20/13 in the right eye and 20/13 in the left eye. Manifest refraction revealed that his present glasses were entirely satisfactory.

Three hundred thousand U. S. P. units of vitamin A was given daily for twenty-six days. Definite subjective improvement occurred at the end of one week of therapy, with slight improvement in final dark threshold. By the nineteenth day the patient was free of all former symptoms, but there was no further change in the dark threshold. For the next twenty-six days he took 150,000 units of vitamin A daily, with apparent marked improvement in his thresholds.

Summary.—This 57 year old white man with subjective evidence of night blindness, even in the presence of a normal dietary, no organic visual defects or other physical ailments, responded to huge doses of vitamin A. Cure was subjective within seven to nineteen days, and marked improvement in the measurable dark threshold occurred by the end of fifty-five days. Improvement was sustained. His sight became better than the average normal.

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34. Supplied by Abbott Laboratories.

PATIENT 2.—L. M., a waitress aged 36, complained of fatigue, falling hair and burning of the vulva. A diagnosis of kraurosis vulvae was made. The patient had been under the observation of Dr. George Gardner for four years for the

CASE I: J.G., Sr.
1. Before treatment
2. 300,000 units Vit.A daily for 1 week
3. "   "   "   "   "   " 19 days
4. 150,000 "   "   "   "   " past 29 days

Mean of 68 normals

Total Vitamin A: 13,150,000 units in 55 days
(Ave. = 239,000 daily)
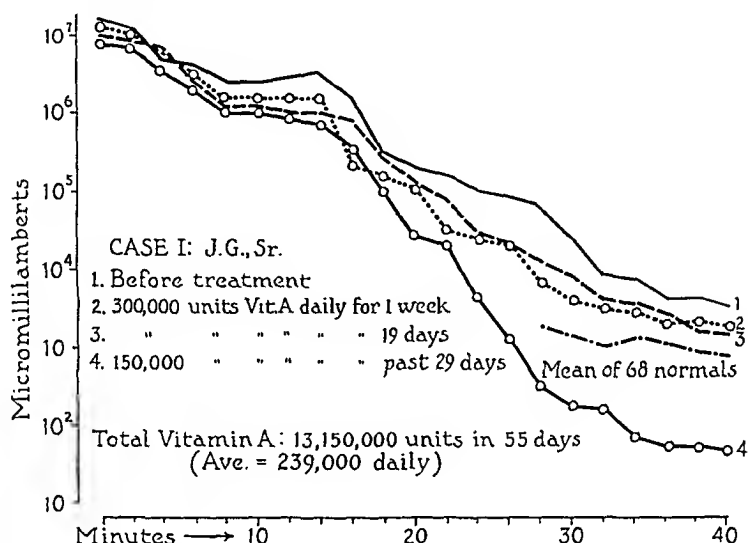
Chart 6.—Effects of large doses of vitamin A. J. G., who complained of night blindness, had a threshold initially not much above the average for normal subjects. After large doses of vitamin A there was subjective improvement, and his threshold on one occasion was much lower (better) than normal.

Mean of
25 normals

L. M. Case 2
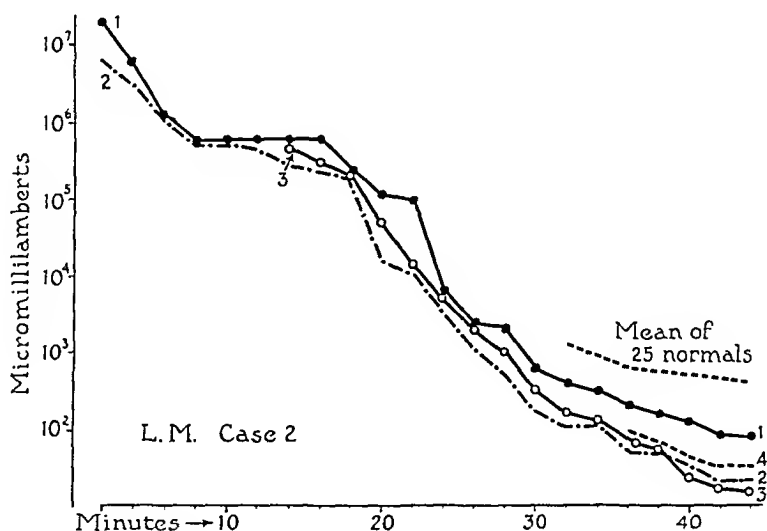
Chart 7.—Effects of vitamin A on L. M., who had typical kraurosis vulvae associated with dark adaptation thresholds lower (better) than normal. Neither the kraurosis nor the dark adaptation showed any effects after 200,000 units of vitamin A daily for three and a half months.

gynecologic condition. Physical examination gave otherwise negative results. The menstrual history was normal. The diet was apparently adequate in all essentials.

Ophthalmologic examination was made by Dr. Helen Holt. No abnormalities were found other than a minute opaque area in the center of the left lens, which was probably of congenital origin. Retinoscopic examination was made under homatropine cycloplegia with a + 1.75 sph. for the right eye and a + 1.50 sph. for the left eye. With a plano lens before the right eye vision was 20/20 + 3; with a + 0.25 cyl., ax. 180 before the left eye vision was 20/15. No glasses were necessary.

Two hundred thousand U. S. P. units of vitamin A was given daily for three and a half months.

Dark adaptation thresholds had always been better than average normal; therefore no effect could be detected during therapy.

Summary.—This 36 year old white woman whose sole difficulty was a characteristic kraurosis vulvae showed no physical, ophthalmologic or dietary evidence of vitamin A deficiency. Dark adaptation thresholds remained unchanged throughout a period of intensive administration of vitamin A. The patient's local pathologic condition was unchanged in spite of the fact that her general state seemed to improve.

PATIENT 3.—H. K., a 60 year old housewife, complained of a vaginal discharge with severe pruritus vulvae and general menopausal symptoms. The menopause had been brought about nine years previously when an operation was performed for fibroid tumors with metrorrhagia. She suffered from chronic cholecystitis with lithiasis, which was kept under control by diet alone. Roentgen therapy to the vulva did not relieve the pruritus. The diet was adequate, but the patient had avoided the use of milk, cream, eggs and butter for the past few years.

Ophthalmologic examination revealed no abnormalities. One and two years before the present period of observation biophotometer tests elsewhere revealed "subnormal visual purple regeneration."

Ten thousand U. S. P. units of vitamin A was given intramuscularly [35] on October 12, 19, 24 and 31 and November 2, 4, 5, 8, 11, 14, 17 and 20. In addition, the patient was given 300,000 units daily by mouth from October 24 to November 11. Oil containing vitamin A was applied locally to the vulva from November 11 to 21.

Summary.—A 60 year old white woman with a severe pruritus vulvae showed no general physical or ophthalmologic evidence of vitamin A deficiency. The diet was low in vitamin A and natural fats. Although the biophotometer tests one and two years previously had revealed poor regeneration of visual purple, her current adaptometer tests gave average normal results. In spite of administration intramuscularly of 120,000 units of vitamin A for over two months, in addition to 300,000 units orally, the visual thresholds became poorer. Local symptoms were temporarily relieved by local application of oil

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35. Supplied by Abbott Laboratories.

rich in vitamin A. It is pertinent that this patient was of a very nervous temperament and fretted considerably over the failure to cure her symptoms quickly with the oil.
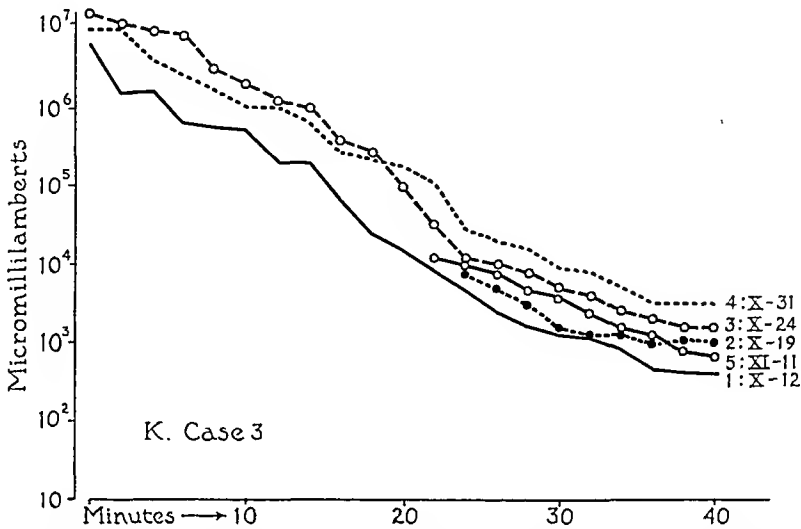
Chart 8.—Effects of vitamin A on K., who had a severe pruritus vulvae associated with normal dark adaptation thresholds. Vitamin A by mouth did not alter her status as measured at intervals from October 12 to November 11.
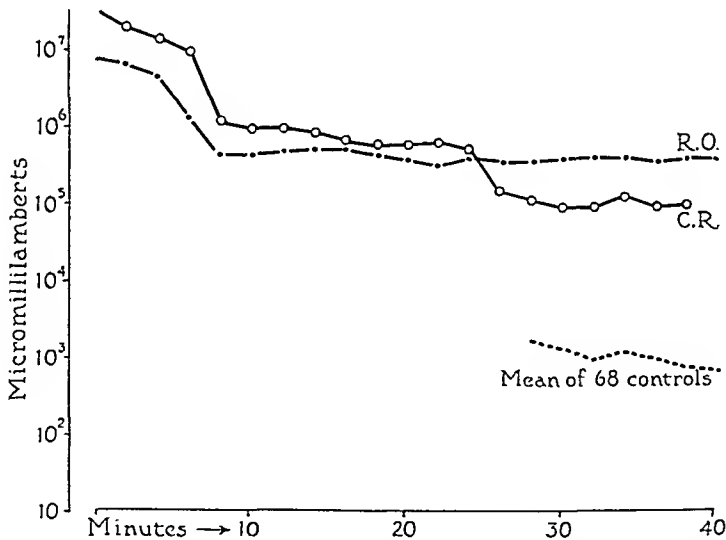
Chart 9.—Two patients with retinitis pigmentosa and definite night blindness gave thresholds much higher than any obtained for subjects on deficient diets. Note that no rod vision is evident.

Dr. Sanford Gifford enabled us to test several subjects who had retinitis pigmentosa. Charts of 2 of these patients are reproduced in order to illustrate the strikingly defective rod vision in this condition.

COMMENT

Two distinct efforts were made to produce vitamin A deficiency in normal young adults.

In the experiment in which liquid petrolatum was used to impair vitamin A absorption, the biophotometer was used to test dark adaptation. The instrument did not prove to be as reliable as we had anticipated. With this instrument it was impossible to detect any correlation between the dietary vitamin A of normal subjects, their biophotometer performance and possibly presumptive clinical signs of hypovitaminosis A. When efforts were made to produce vitamin A deficiency with large doses of liquid petrolatum in these subjects, no statistically reliable evidence of deficiency was detected by photometric measurements; nor were there ever any signs and symptoms of vitamin A deficiency. Supplements of oil concentrates which provided 200,000 units of vitamin A and 2,700 units of vitamin D daily produced no apparent change in any of the subjects.

The second experiment was more accurately controlled through the use of a satisfactory photometer and by rigid supervision of diet.

It was observed that the 3 subjects who lived on a deficient diet for forty-three, forty-nine and forty-nine days, respectively, failed to show more than a suggestion that their stores of vitamin A were being depleted as determined by dark adaptation levels. The subjective symptoms reported by one subject (G) suggested a possible temporary hypovitaminosis beginning on the fourteenth day. Another subject (S) reported suggestive symptoms on the sixteenth to forty-second days, although his dark threshold was never greatly elevated. The third subject never gave any evidence of a deficiency.

Table 4 indicates that the literature now contains, with the present report, reports from seven groups of observers. All have tried to produce vitamin A deficiency in human subjects through limitation of the dietary intake of vitamin A. Twenty-two different persons have been maintained on diets containing from 50 to 300 units of vitamin A daily for periods ranging from twenty-five days to six months. The subjects have been tested for signs of impaired dark adaptation by the same or by a similar apparatus under similar experimental conditions. It is significant that each group has reported a difference in the time at which signs of possible deficiency appeared. One group [32] found no evidence other than histologic changes in the skin after six months on the deficient diet. We interpret our results to indicate a failure to produce a definite evidence of deficiency after forty-nine days on a daily diet containing 74 units of vitamin A. Our subjects must either have had a large store of vitamin A or were very unsusceptible, or it takes a long time to manifest definite evidence of deficiency. Another group [29] referred to the production of recognizable changes

in dark adaptation after twenty-four hours on a diet, with more pronounced signs after eight days.

Restoration of vitamin A has been attempted by administration of oil concentrates in doses varying from a single dose of 8,500 units to 300,000 units daily for several months. The results with this form of therapy have been even more variable than have been the signs of the depletion.

TABLE 4.—*Summary of Published Data on Attempts to Induce Dietary Vitamin A Deficiency in Adults*

Observers	No. of Subjects Sex	Vitamin A (U. S. P. Units)	Threshold Change	Supplement	Results
Hecht and Mandelbaum	4 ♂	150 daily	10th day to 30th day	50,000 units of vitamin A daily	Subjects not back to normal by 75th day; single dose of 100,000 units of vitamin A caused improvement same day
Wald, Jeghers and Arminio	1 ♂	50 to 200 daily	1st defect in 24 hr.; 4th day definite to 25th	100,000 units of vitamin A	Single dose caused improvement in 24 to 150 min. with night blindness again by 2d day; single dose of carotene (100,000 units of vitamin A) produced normal readings in 38 to 80 min.
Booher	5	93 to 103 daily supplemented with thiamine, riboflavin, iron, iodine and viosterol	29 days 27 16 124 39	Cod liver oil and carotene	Single dose of cod liver oil caused improvement in 2 to 3 hr. which lasted for 24 hr.; daily administration of cod liver oil in amounts less than that required for cure for 2 to 3 weeks finally produced a stationary state
Steffens, Blair and Sheard	2 ♂	100 to 300 daily	None after 6 mo.	....	80,000 units of vitamin A daily to 1 subject caused no change; thresholds fell slightly on diet but rose again without supplement of vitamin A
Pett	1 ♂	50 for 37 days	18th day (anorexia); 33d to 35th day (night blindness)	Vitamin A	Single dose of 8,500 units of vitamin A caused improvement in 2 hr.; equal dose of carotene caused improvement in 5 hr.
Steininger * and Roberts	6 ♀	100 (under) daily	25th and 44th days	Vitamin amount varied	Only 2 of 6 showed depression of biophotometer thresholds after 2 wk.; both of these dropped rapidly thereafter; improvement doubtful on vitamin A supplement
Isaacs, Jung and Ivy	3 ♂	74 daily	Never definite	300,000 units daily	See summary

* These were the only observers to use the biophotometer.

We have included 3 case reports from our clinical records to demonstrate the different types of response which may be obtained in potentially vitamin A–deficient persons. One of these patients received large doses of vitamin A intramuscularly to test the theory that disease of the biliary tract may lessen or prevent absorption of orally administered vitamin A. No difference could be detected between the effects of oral and of intramuscular therapy in this patient or in other patients followed.

In view of the fact that several observers have reported a probable vitamin A deficiency among the general population, amounting in some

areas to as high as 52 per cent, it seems advisable to consider the meaning of this. The possibilities which occur to us are, first, that the average American diet may be deficient in available vitamin A or its precursors; second, that the standard of vitamin A intake on which subjects are judged to be deficient is questionable, and third, that the procedures being used for measurement are recording something other than vitamin A deficiency. We incline toward a combination of the latter two possibilities.

A large subjective factor is involved in the determinations obtained in all types of visual tests. It is our opinion that the subjective factors should be recognized and an attempt be made to control them when measurements of dark adaptation levels are made; also, that significance should not be attached to minor fluctuations in dark adaptation in terms of vitamin A deficiency unless statistical methods are used to test the reliability and validity of differences.

SUMMARY

The adaptometer as designed by Hecht has been found to be more reliable for the determination of visual dark adaptation thresholds than the biophotometer.

Relatively large doses of liquid petrolatum (5 cc. per kilogram of body weight) daily for periods up to as long as one hundred and thirty-one days failed to produce recognizable vitamin A deficiency or other unfavorable effects in 28 normal young adults. These subjects were compared during the same period with 29 normal young adults who did not receive the liquid petrolatum.

A diet containing an average of 74 U. S. P. units of vitamin A daily failed to produce definite measurable visual evidence or subjective signs of deficiency in 3 subjects maintained on the diet for forty-three to forty-nine days. Temporary subjective clinical evidence of deficiency was reported on the fourteenth and sixteenth days by 2 subjects, but none was reported by the third subject.

Normal subjects showed the same trend toward increased dark threshold levels between September and December that was manifested by the subjects on the controlled deficiency diet. The possible explanation for this is discussed.

Measurements of vision, size and shape of the physiologic blind-spot and of visual fields failed to indicate consistent significant changes which could be attributed to vitamin A deficiency or to high vitamin A therapy.

Doses of 300,000 units of vitamin A daily for as long as four months failed to show evidence of harmful effects in the 3 experimental subjects on the deficient diet regimen. The same dose occasionally failed to improve the dark thresholds in 10 patients suspected of having vitamin A deficiency.

FUNDAMENTAL DIFFERENCES BETWEEN CROSSED CYLINDER AND LINE CHART ASTIGMATIC TESTS

JOSEPH I. PASCAL, M.D.

NEW YORK

The two most commonly used subjective methods for testing astigmatism are (1) the various tests involving the use of some form of line chart and (2) those involving the use of the crossed cylinder. Sometimes, of course, both methods are combined. I am not going into the how and why of these tests except incidentally. My prime purpose is to discuss some points of fundamental differences between them. These differences are not discussed in any of the standard works on refraction, and yet they have theoretic and practical significance.

In the uncorrected astigmatic eye there are two focal lines formed for every point of the object seen. These lines correspond to the two principal meridians, are at right angles to each other and are at different distances. The space between them is the interfocal distance, better known as Sturm's interval. But the retinal images do not necessarily consist of these focal lines. Only one of these lines could possibly fall on the retina; the other line must then be either in front or behind. Or neither of these two focal lines may fall on the retina.

If both focal lines are in front of the retina, as in compound myopic astigmatism, real or artificial, the retinal image of a point will be an oval diffusion spot and the retinal images of all objects seen will be made up of oval diffusion spots. If both focal lines are behind the retina, as in compound hyperopic astigmatism, the retinal images will likewise be made up of oval diffusion spots. If one focal line is on the retina and the other in front or behind, as in simple myopic or hyperopic astigmatism, the retinal images will be made up of what may be called diffusion lines. In the special case in which one focal line is in front and the other behind the retina, as in mixed astigmatism, real or artificial, there are two different conditions to consider. If the two focal lines are at different distances from the retina, the retinal image will consist of oval diffusion spots similar to those of compound myopic or compound hyperopic astigmatism. But if the two focal lines are equally distant from the retina, i. e., practically equally distant, the retinal images

will consist of diffusion circles. In this instance, and in this instance only, will the retinal diffusion spots in an astigmatic eye be exactly like the retinal diffusion spots in an eye with a spherical error, i. e., in simple myopia or simple hyperopia. The significance of this will be seen later.

A word about the effect of lenses on the absolute and relative positions of the two focal lines. A spherical lens will move both lines forward or backward, a plus lens forward and a minus lens backward without essentially altering their relative position to each other. But this movement may alter completely the size and shape of the retinal diffusion spots which alone compose the image of the object seen. A cylindric lens placed with its axis in one of the principal meridians will move only one focal line and will therefore increase, decrease or abolish the interfocal distance. A cylindric lens with its axis oblique to the principal meridians will create new conditions. It will give rise to a new pair of focal lines which will differ in direction from the old pair of focal lines and at the same time generally change the absolute and relative positions of the new focal lines. The precise effect depends on several factors and can be determined for any set of conditions.

There are three steps in a test for astigmatism: 1. One should find whether or not there is any astigmatism. 2. If there is astigmatism, one should locate the correct axis. 3. The amount of the astigmatism is then determined. The line charts and also crossed cylinder can be used for all these three steps. But the crossed cylinder has a number of additional uses, such as determining the best relative distribution of sphere and cylinder, testing for inefficient accommodation and checking the presbyopic addition. These other tests, however, are not considered in the present paper.

TESTS FOR CORRECTIBLE ASTIGMATISM

By correctible astigmatism, the presence or absence of which is determined in the first step of a test, I mean astigmatism which when corrected will enhance the patient's vision or comfort. By the line charts, the presence of astigmatism is indicated by the difference in the clearness of a set of radiating lines. It is generally said that the observation should be made with the eyes fogged, that is, made artificially myopic if the eyes are not naturally myopic. By bringing both focal lines in front of the retina, the retinal image will consist of ovals, and those ovals running in the direction of some one line on the chart will make that line stand out plainer. Generally, however, instead of a full fog, that is, with both focal lines in front of the retina, the difference in the lines is more easily perceived when one focal line is on the retina and the other in front. The clearest line stands out more sharply when the eye is only half fogged. But if the eye is in a mixed condition, i. e., if one focal line is in front and the other behind the retina and at approxi-

mately equal distances, then the astigmatism will not show itself by the line chart method at all. The diffusion spot on the retina, being a diffusion circle, will form similar images of all the radiating lines, so that none will stand out. One may therefore say as a first premise that for the line chart to disclose the presence of astigmatism the eye may be fully fogged, or preferably it should be only half fogged; however, it must not be in a mixed condition. By a mixed condition I mean a condition of mixed astigmatism where one meridian is myopic and the other hyperopic, so that one focal line is in front of the retina and the other behind the retina. When the eye is in a mixed condition the test with the line chart is definitely misleading. A spherical lens can be used to produce whatever condition of full fog, half fog or mixed condition is desired.

The crossed cylinder method of determining the presence of astigmatism is to twirl the crossed cylinder before the eye while it views the smallest letters and have the patient compare the effect of either position. If one position is preferred over another, astigmatism is indicated. The basis of the test is the improvement in general focusing produced by a cylinder, which though approximate in strength and position does correct some of the astigmatism present, or rather it corrects the astigmatism fully or partly when it is in one position and increases the astigmatism when it is in the other position. If an eye has only a spherical error, the application of the crossed cylinder in any position creates a certain amount of astigmatism, which is the same for any position of the crossed cylinder. Therefore, vision will be about the same in the several positions tested. But if there is any astigmatism the crossed cylinder will tend to increase it in one position and diminish it in another, so that there will be a difference in vision.

It is generally said that this is best done when the eye is fogged; but in practice the test when the eye is fogged is often difficult, and a little analysis will show why. For example, suppose there is a natural or artificial myopic astigmatism of 0.50 D. and the eye is fogged 0.50 D. Both focal lines are in front of the retina; one focal line is 1.00 D. in front and the other is 0.50 D. in front. It is easiest to indicate the position of the focal lines by the refraction of the meridians corresponding to these focal lines (fig. 1).

The retinal image before the crossed cylinder is applied consists of oval diffusion patches 0.50 D. by 1.00 D. If a ± 0.25 crossed cylinder is now used along the principal meridians, in one position it will separate the focal lines by 0.50 D., i. e., bring one 1.25 D. in front of the retina and the other 0.25 D. in front (fig. 2). The retinal images will now consist of long ovals, 0.25 D. by 1.25 D. In the other position the crossed cylinder will bring the two focal lines together, producing an

error of 0.75 D. sphere (fig. 3). The retinal images will consist of diffusion circles 0.75 D. by 0.75 D. The patient has to compare images (fig. 2 and fig. 3) produced by different kinds of diffusion spots, one an oval 0.25 D. by 1.25 D. and the other a circle 0.75 D. by 0.75 D. The latter is like the diffusion circle in 0.75 D. of myopia or hyperopia. It will be rather difficult for the patient to choose. In fact, some letters
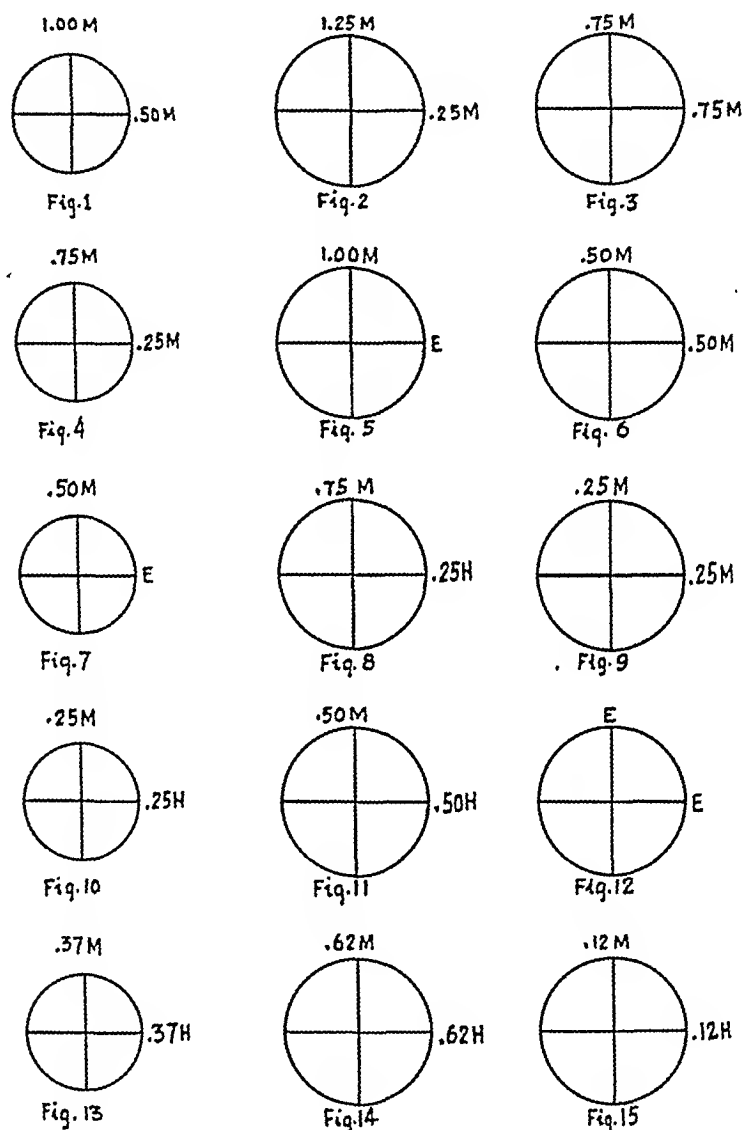
Figs. 1–15.—Diagrammatic representation of the refractive conditions resulting from each of the two positions of the crossed cylinder. From these one can visualize and compare the relative size and shape of the diffusion spots forming the retinal image.

may appear better under a blur of 0.25 D. by 1.25 D. than under a blur of 0.75 D. by 0.75 D., giving a totally incorrect clue to the condition.

Suppose the eye of this same subject is slightly fogged 0.25 D. There are then 0.75 D. of myopia in one meridian and 0.25 D. in the other meridian (fig. 4). The retinal images will consist of blurs of 0.25 D.

by 0.75 D. to start with. With the crossed cylinder in one position, one gets 1.00 D. of myopia in one meridian and emmetropia in the other (fig. 5), and in the other position one gets 0.50 D. of myopia in both meridians (fig. 6). The patient has to compare retinal images made up of 1.00 D. line spots with retinal images made up of blurred circles of 0.50 D. by 0.50 D. Whether one or the other will be preferred will depend on the contours of the letters seen and other factors. But the change in vision will certainly not be definite and clearcut.

Suppose the eye is half fogged, i. e., one focal line is on the retina and the other is 0.50 D. in front (fig. 7). The retinal images now consist of line spots to begin with. With the ± 0.25 crossed cylinder in one position, the focal lines are separated, so that one is 0.75 D. in front and the other 0.25 D. behind the retina (fig. 8). This gives diffusion spots 0.25 D. by 0.75 D. In the other position one focal line is 0.25 D. in front of the retina and the other also 0.25 D. in front, giving a diffusion spot of 0.25 D. by 0.25 D., the same as in 0.25 D. of myopia. Here the difference in vision should be readily noted, because vision with the circular diffusion spots will be better than with the oval diffusion spots. But even here, the diffusion spots being different in shape, a small circle 0.25 D. by 0.25 D. in one case and a small oval 0.25 D. by 0.75 D. in the other, the differences in the clearness of the retinal images will be partly obscured by the difference in the shape of the diffusion spots producing these images.

Suppose now this condition is changed to one of mixed astigmatism, i. e., one focal line is 0.25 D. in front of the retina and the other is 0.25 D. behind the retina (fig. 10). The retinal images before interposition of the crossed cylinder consist of diffusion circles of 0.25 D. by 0.25 D. The effect of the crossed cylinder is as follows: In one position it separates both focal lines, so that one is 0.50 D. in front of the retina and the other 0.50 D. behind (fig. 11). This produces retinal diffusion circles of 0.50 D. by 0.50 D. In the other position it brings the two focal lines together on the retina and to a point focus (fig. 12). The difference in vision is striking—exactly the same as when a — 0.50 D. sphere is placed before the eye of a person with low myopia. Even when the crossed cylinder does not change the blurred circle to a point focus as in figures 11 and 12, the difference in vision will still be striking. Suppose the astigmatism is 0.75 D. instead of 0.50 D. If a similar analysis is carried through one will find that when the retina is in the midway position (fig. 13) the ± 0.25 crossed cylinder changes the retinal diffusion spots from 0.62 D. by 0.62 D. to 0.12 D. by 0.12 D. (figs. 14 and 15). Here the retinal images in the two positions of the crossed cylinder are composed of the same type of diffusion spots, i. e., diffusion circles. In one position of the crossed cylinder the diffusion

circles are 0.62 D. by 0.62 D., and in the other position they are much smaller, 0.12 D. by 0.12 D. The retinal images made up of the tiny diffusion circles will certainly be strikingly clearer. Here again the effect is exactly like placing a — 0.50 D. sphere before the eye of a person with low myopia. It is instructive to carry through a similar analysis for different amounts of astigmatism and different powers of the crossed cylinder used.

Suffice it to say that for the determination of the presence of astigmatism with the crossed cylinder, best results are obtained when the eye is placed in an equally mixed condition, that is, when the retina is practically half way between the two focal lines. If the eye is fully fogged, even to a slight extent, results are difficult to obtain and are not reliable; if the eye is half fogged, results are better, somewhat similar to the improvement produced by a weak minus cylinder. But if the eye is in a mixed condition, the change in vision produced by flipping the crossed cylinder is sudden and striking. The improvement in vision is similar to that produced by placing a weak minus sphere before the eye of a person with low myopia. All this, as will be recalled, is exactly the reverse of the findings with the line charts.

The relative merits of these two methods, i. e., line chart and crossed cylinder, is a matter of opinion, naturally. Some patients respond more readily to one test than to another. The line chart method permits simultaneous comparison of the lines as they are gradually cleared up with the reduction of the fog. This gradual, simultaneous observation method may be good for some patients. But the sudden, striking change produced by the crossed cylinder is in my opinion more reliable as a test for correctible astigmatism—the kind of astigmatism that endures and not the kind that is here today and gone tomorrow. It is also by far the better method when a certain amount of regular astigmatism is obscured by an excessive amount of irregular astigmatism.

TESTS FOR CORRECT AXIS

The second step in the determination of astigmatism is to locate the accurate axis. The approximate axis is found by either method at the same time that the presence of the astigmatism is found. With the line chart method the accurate axis is generally located either by the use of the revolving V or by rotating the cross line. By the V method, the correct axis is determined when the two limbs of the V appear equally clear or equally blurred. In the absence of a V pointer, the line on the cross is rotated either way, to determine when it appears blackest. In both of these tests it is best that the eye be half fogged. Full fogging makes the test less delicate, and a mixed condition makes it unreliable.

To find the accurate axis by the crossed cylinder method, a moderately strong cylinder, say + 1.00, is first placed at the axis found by the first test. The crossed cylinder is then placed with its axes at 45 degrees to the test lens axis and rapidly flipped from one position to the other. If the axis of the test cylinder is right, vision will be the same with either position of the crossed cylinder. But if the axis position of the test cylinder is incorrect, vision through the crossed cylinder will be different for the two positions. The axis of the test cylinder is then turned in the proper direction, and the test is repeated in the new position of the test cylinder. For this test it is best if the eye is fully fogged to a slight degree before interposition of the crossed cylinder. The effect of the crossed cylinder here is to distort the retinal image spots, and if the position of the axis is incorrect, the crossed cylinder distorts them more in one position than in the other.

The relative merits of these different tests for determining the accurate axis are these: With the revolving V, a simultaneous comparison can be made of the two limbs, which is sometimes an advantage. The revolving cross chart produces gradual changes which are difficult to observe. The crossed cylinder gives a sudden change of effect and is generally more striking. The optical effect is similar to, but much better than, the method of rotating a test cylinder from its approximate position in either direction to the point of equal blur and choosing the position midway between the extremes as the correct position. In fact, one of the principal uses of the crossed cylinder is for the accurate determination of the axis. One can readily check the efficiency of the crossed cylinder for this purpose by turning the test cylinder, say, 10 degrees, and checking the effect with the crossed cylinder. Incidentally, some knowledge of transposing obliquely crossed cylinders makes testing with the crossed cylinder more meaningful. Nor does such oblique transposition require any mathematics, as there are simple, completely nonmathematical methods for doing such transposition.

TESTS FOR AMOUNT OF ASTIGMATIC ERROR

The third step is to find the amount of astigmatic error. By the line chart method the amount is determined when the lines on the cross are equalized by a cylinder. For this test the eye should be preferably fully fogged to a slight degree, about 0.25 D. When it is so fogged, a slight overcorrection will be shown by reversal of the clearest line. The eye may be half fogged, but it must not be in a mixed condition, as this will lead to erroneous results. By the crossed cylinder method the crossed cylinder is flipped back and forth with its axes corresponding to the axis of the test cylinder while the patient notes the effect of the sudden changes on his vision. Here the best results are obtained when the

eye is not under fog, either half or full, but when the retina is in the midway position. In this position the contrast is most marked. and the patient's reactions most easily obtained. To sum up, the test is most unsatisfactory when the eye is fully fogged, less so when it is half fogged and best when it is in a mixed condition. Again it is shown how different this is from the line chart method. A combination of line chart and crossed cylinder is often effective at this stage.

COMMENT

I said before that the first step in an astigmatic test is to determine the presence or absence of correctible astigmatism. Now every patient almost without exception can be given a weak cylinder if the examiner is bent on it and tries hard enough. But I think a cylinder so given is neither necessary nor desirable. I am afraid that the ophthalmologist has come to look on refractive errors too much as definite static entities similar to the trial lenses. A + 0.25 sphere is the same today as it was last year and as it will be next year. It is exactly the same to half a dozen different examiners who may use it. But a refractive error, especially a low cylindric error with or without a spherical error and determined with difficulty, is not such an entity at all. The same examiner will find slight differences if he examines the same patient on different days or at different hours of the day. Different examiners, all working conscientiously and even using similar methods, will find slightly different corrections, the differences running anywhere from 0.12 to 0.50 D. with similar variations in the position of the axis. The mental and physical states of both patient and examiner are bound to modify the findings, and all of these corrections will probably be equally satisfactory, all falling within the dynamic physiologic and psychologic limits of the visual function. To regard refractive errors otherwise, that is, as precise entities to be corrected as such, is contrary to the knowledge of general human physiology and psychology and is certainly incompatible with the knowledge of the physiology and psychology of vision; to mention only the depth of focus which is found in every eye, the inevitable ocular aberrations which preclude perfect focusing and the constant changes in the size of the pupil which although grossly tending to improve focusing certainly do not do it with mathematical accuracy. Then again the inevitably small errors introduced by combining a mobile eye with a fixed lens, the change of effectivity in a lens when used for far and near vision, vitiate any attempt at precision focusing. One can readily see by dynamic retinoscopic examination and other tests that even when the eyes are reading very fine print at some near distance, say 13 inches (33 cm.), they are not exactly focused optically for that

distance. In fact, it was to emphasize this point that I introduced some years ago the term "physiologic focusing" as distinct from "optical focusing."

I believe in general that only the astigmatism which is definite, which is more or less easily found by quick and decisive reaction on the part of the patient, should be corrected. Of course every patient has what may be called a coefficient of reaction; some persons are naturally quicker than others, but within their own coefficient of reaction one should distinguish between the genuine response and the laborious, studied reply. In this respect, perhaps, the crossed cylinder lends itself especially well for determining the presence of true, correctible astigmatism as against the pseudo variety. But there is no one test which will always work. One will find persons who respond best to the line chart methods and others, I believe a far larger number, who respond best to crossed cylinder methods. What is important is to understand the basic differences between the various tests as I have tried to explain. Knowledge of the conditions under which each test is most reliable will enable one to utilize them all more effectively.

ORBITAL APEX AND SPHENOID FISSURE SYNDROME

HELEN HOLT, M.D.

CHICAGO

AND

A. DE RÖTTH, M.D.

SPOKANE, WASH.

We wish to call the attention of ophthalmologists to the orbital apex–sphenoid fissure syndrome which, though not rare, has not yet been described in the American ophthalmologic literature under this title so far as we know. Patients with this syndrome seek the aid of the ophthalmologist, and if the symptoms are not correctly interpreted, an intracranial lesion may be assumed to be present.

The syndrome is due to an inflammatory, neoplastic or traumatic process involving the nerves going through the sphenoid fissure: the third, fourth and sixth cranial nerves, the ophthalmic branch of the fifth cranial nerve, sympathetic fibers and the optic nerve at the orbital apex. This causes an impairment of vision of varying degrees, depending on the amount of pressure on the optic nerve. Defects of the visual field will depend on the same factor. The ophthalmoscopic findings may vary from the normal to marked optic neuritis and later atrophy of the optic nerve. Further symptoms are: ptosis; diplopia; ophthalmoplegia, in which all or a part of the external muscles of the eye are involved but in different degree; a wide pupil with loss of accommodation; hyperesthesia or anesthesia of the upper lid, half of the forehead and the cornea, and vasomotor disturbances. All these symptoms differ a great deal according to which nerves are involved. Pain is a fairly constant and early symptom; it is localized behind the eyeball and radiates to the top of the head, the forehead and temples, usually subsiding when the ophthalmoplegia is at its height. Exophthalmos is not constant and is of small degree.

In the last few years we have observed 3 cases of this syndrome caused by an infectious process.

Case 1.—K. I., a youth aged 17, had been in good health until September 1933, when he began to suffer from severe headaches, chiefly in the right half of the forehead and right temple, associated with nausea and vomiting several times a day. There were periods of several days when he was free from symptoms. In

October 1933 he noticed that the right eye was watering and that the upper lid was tender and sometimes swollen. Soon after, ptosis and diplopia developed, and the vision of the right eye rapidly diminished. His parents, two brothers and two sisters were in good health. On November 25 he was admitted to the neurologic service of St. Stephens Hospital, Budapest. There was no perception of light in the right eye, and the vision of the left eye was 5/5. There was exophthalmos of the right eye of 2 mm. with ptosis. Motility of the eye was restricted in abduction and infraduction, with no movement up and in. The pupil was wide and inactive. The retinal veins were slightly dilated, and the nasal half of the margins of the disk was hazy. The left eye was normal. Medical, neurologic, rhinologic and otologic examinations gave negative results; the blood and spinal fluid were normal. A roentgenogram of the skull did not show any pathologic involvement. On December 9 the right disk was pale. Potassium iodide, aminopyrine and salicylates were given. On December 28 ptosis and ocular motility were much improved. In May 1934 there was perception of light in the right eye.

In September 1934 ptosis appeared on the left side, and ocular motility was impaired. Pain began in the left orbit soon after, associated with left-sided headaches and vomiting, as in the previous year. On December 6 the patient was admitted to the State Eye Hospital of Budapest. The vision of the right eye was limited to counting of fingers at 1½ foot (45 cm.); the vision of the left eye was 5/5. In the right eye there was no ptosis, motility was free and the pupillary reaction was sluggish. The disk was pale, with the margins slightly hazy. Retinal vessels going downward showed white bordering streaks beyond the margin of the disk. A small crescent was present in the periphery of the nasal portion of the field. The left palpebral fissure in the primary position was 9 mm. wide and the right 11 mm. Abduction of the left eye was nearly normal, but supraduction and infraduction were impaired and adduction was absent. The pupils were normal and reacted well. The fundus was normal. The fields for white and for color were normal. The left eye protruded 0.5 to 1 mm. Medical, neurologic and rhinologic examinations revealed no other pathologic process. The reaction to an intradermal injection of tuberculin was negative, as was the Wassermann reaction. Roentgenograms revealed equal and normal optic canals, but the left sphenoid fissure was markedly smaller than that of the right side, as shown in the accompanying illustration. On the basis of this roentgen finding, we assumed that there was a lesion of the left sphenoid fissure of inflammatory origin, probably periostitis because of the pain, the occasional swelling of the upper lid and the tenderness when the eye was pushed backward. No evidence of the causation of the supposed periostitis could be made out. The disease ran a favorable course, and all the symptoms of the left side subsided in six weeks.

Case 2. — Mrs. F. L., 32 years of age, had been suffering from diseases of the eyes since early childhood; first, a phlyctenular keratoconjunctivitis, and later, scleritis and sclerosing keratitis. In 1931 a fistula developed in an intercalary staphyloma of the right eye. Several operations to close the fistula were performed in the State Eye Hospital of Budapest, the last of which, in February 1933, gave a favorable result. On June 14, 1935, the patient reported that she had had a severe right-sided headache with the pain centering around the right eye. She felt as though something were pushing the eye forward, and she suffered severe pain when the eye was pushed backward. During the last days right-sided ptosis appeared, and there was hypesthesia of the upper lid and the right half of the scalp and forehead. The vision of the right eye was 5/12; with a 2.50 sph. it was 5/8. The vision of the left eye was limited to counting fingers at 10 feet

(305 cm.) ; with a — 6.00 sph. ⊃ — 2.00 cyl., ax. 170 it was 5/25. She had the same vision in February 1933, after the scleral fistula of the right eye was closed. There were transparent maculas in each cornea and transparent scleras around the corneas due to the diffuse scleritis. The left eye was otherwise normal. In the right eye there was diminished sensibility of the cornea, and the pupil was irregular, due to the old uveal prolapse into the fistula of the intercalary staphyloma. There was marked ptosis, and motility of the right eye in all directions was only 3 to 5 degrees. The disk was slightly edematous, with indistinct borders as a result of the choked disk, which lasted for nearly two years, accompanying the scleral fistula. The right eye protruded 0.5 to 1 mm. A roentgenogram showed a slight shadow in the area of the right sphenoid fissure as contrasted to the appearance of the left side.

On July 19 the patient reported that she had been suffering for two weeks from a peripheral facial palsy on the left side. Protrusion of the right eye had slightly
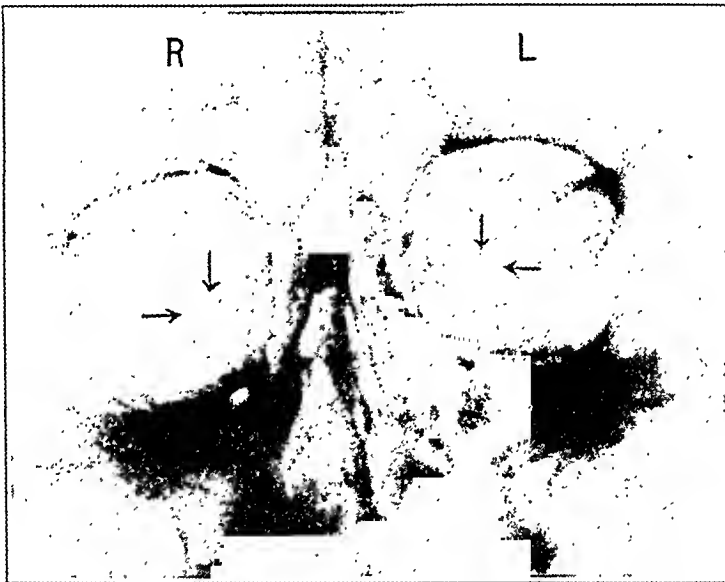
Roentgenogram showing the left sphenoid fissure to be markedly smaller than the right.

increased; motility had not improved, but the headache was less. The administration of tebeprotin (Toennisen), a human tubercle bacillus protein, solution 2, 0.1 cc. intradermally, gave a positive reaction. We assumed that there was tuberculous periostitis at the sphenoid fissure. In a surgical clinic a diagnosis of a sarcoma of the sphenoid bone was made and operation proposed. Our treatment consisted in the injection of 0.2 cc. of tebeprotin (Toennisen), solution 3, at intervals of five days. In December 1935 all paralytic symptoms had subsided.

Case 3.—Mrs. M. K., aged 35, entered the ophthalmic clinic of Northwestern University complaining of blurred vision in the right eye, drooping of the lid and continuous dull aching in the right side of her head. Six weeks previously she had had a violent right-sided headache, which came on suddenly and continued unabated for one month. Even the scalp was extremely sensitive to touch. As this subsided the right upper lid began to droop, and the eye became fixed in the forward position. Vision failed rapidly, so that within a period of two weeks print became invisible. No vomiting or generalized symptoms were associated.

A similar train of symptoms with the addition of diplopia occurred on the left side two years previously, resulting in blindness of the left eye but recovery of motility of the eye and lids. No Jaeger test type was visible except when a + 3.00 sph. was held before the eye, then Jaeger's test type 2 was read with ease. There was no perception of light in the left eye. In the position of rest, the right upper lid covered two thirds of the cornea. When an attempt was made to raise this lid, the right eye remained motionless and the left turned up and in. The right pupil measured 6 mm. and the left 3 mm., and both remained fixed to light and in accommodation. Right corneal sensitivity was diminished. Pressure on the right eyeball caused considerable pain. The right eye protruded 3 mm. beyond the left. The right disk was a little blurred on the nasal side but could be considered within the variations from the normal. The left disk was gray-white, with sharp margins, and fine connective tissue was present along the vessels on the disk. The right fields, both central and peripheral, were normal. The Wassermann and Mantoux tests of the blood were negative. The temperature was 99 F. The condition was considered a nonspecific periostitis at the sphenoid fissure, and the patient was admitted to the Passavant Hospital for foreign protein therapy.

Two injections of typhoid vaccine were given, and the patient had severe reactions to both. Spinal puncture revealed no increased intracranial pressure, and the spinal fluid was normal in all respects. A spinal puncture at another institution one week previously had given similar findings. Four days after the second injection of typhoid vaccine was administered, a subtemporal exploratory operation was performed by Dr. John Martin, since Dr. Loyal Davis and Dr. Martin considered the cause of the symptoms to be a paratrigeminal lesion. At operation no pathologic changes were found in this region, but about the sphenoid fissure the dura was raised in small rounded mounds which were spongy on pressure, with the surface smooth, shiny and unbroken. No tissue was removed for fear of excessive bleeding, and the wound was closed in the usual manner. The patient made an uneventful recovery and on examination in the clinic on Aug. 28, 1939 the vision of the right eye was 20/25 — 3 uncorrected; exophthalmos was 1.5 mm.; motility had returned to about half of normal; the fields were normal.

On September 20 ocular motility was normal in all directions; no ptosis was present; exophthalmos was nil and the vision of the right eye was 20/20 with ability to read Jaeger's test type 1. The only discomfort the patient noted was a tingling and a sensation of heat over the area of distribution of the ophthalmic branch of the right fifth cranial nerve. Objectively the skin was redder and warmer to touch than in a similar area on the left side.

The patient has remained in good health and has returned to factory work. Subsequently, her record of two years previous was obtained from the Cook County Hospital. The blood and spinal fluid then gave a positive Wassermann reaction, and the condition was diagnosed as syphilitic basilar meningitis. Mercury and iodide therapy were given during her stay at that hospital.

With regard to the infectious syndrome in this case, the first attack was considered syphilitic and the second nonsyphilitic. The second may have been an occult form of the disease, as described by Roger and Alliez, or a nonsyphilitic infection.

In addition to these cases, a case in which the syndrome was due to a malignant growth is presented, illustrating the complexity of the symptoms and clinical findings and the atypical progress of the syndrome with this causation.

Case 4. — Mr. B. S., aged 29, was referred to the clinics of Northwestern University on Feb. 21, 1939 for a special neurologic study. For nine months he had been unable to move the right eye upward, downward or to the right. During this time a corneal ulcer had developed which was treated with injections of typhoid vaccine and calcium. From the neurologic examination it was determined that the right second, third, fourth, fifth, seventh, eighth and ninth cranial nerves were involved. A diagnosis of postinfectious polioencephalitis was made. On April 13 there was no evidence of a neoplasm on roentgen examination, and the spinal fluid was normal in all respects. March 20 the patient was seen in the ophthalmologic clinic of Northwestern University. The vision of the right eye was 20/200 and blurred, and the patient was not able to read any Jaeger's test type. The vision of the left eye was 20/13, and the patient could read Jaeger's test type 1 at 13 inches (33 cm.). Heterochromia of the irides was noted. There was incomplete ptosis of the right lid. The right eye moved nasally but would not move past the midline temporally and moved up and down only partially. Superficial opacities in the lower half of the right cornea were noted at the site of the recent ulcer. Right corneal sensitivity was completely abolished. The pupil reacted to light and in accommodation. The fundi were normal. The right field was contracted to 30 or 40 degrees and the left to 60 degrees. No definite diagnosis was made.

The patient was not seen again in the ophthalmologic clinic until July 21, when he reported that the vision of the right eye had suddenly decreased to nil two weeks previously. There was complete internal and external ophthalmoplegia of the right eye. Since the lens had become uniformly cloudy and the cornea was slightly opaque, details of the fundus could not be made out. The left eye remained normal in all respects. A diagnosis of a right paratrigeminal lesion, either a tumor or a vascular lesion, was made by the examining neurologist, and the patient was operated on in'August 1939 by Dr. John Martin. A basilar meningioma was found extending from the frontal fossa to an undetermined point posteriorly. Only a small portion could be removed. When the patient was seen on September 22 the right ophthalmoplegia remained; although the vision of the left eye remained 20/13, the field was contracted to 20 degrees. The disk was elevated 1.5 diopters, the veins were engorged and many superficial retinal hemorrhages were present. Intracranial pressure was increasing as the tumor became more extensive. Further changes will depend on the direction of growth of the mass. The outcome is hopeless.

COMMENT

There were observed 3 cases of the orbital apex–sphenoid fissure syndrome due to an infectious process; in cases 1 and 3 the syndrome was complete and in case 2 there were only the symptoms referable to the sphenoid fissure without involvement of the optic nerve. In 2 of the cases (1 and 3) the involvement was bilateral, but during the acute stage of the disease in the first eye the patients were not under

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our observation. The interval between the onset in the first and the second eye was one year in case 1 and two years in case 3. Two men and one woman were affected, their ages being 17, 32 and 35 years. The causation could be stated with great probability as tuberculosis in case 2, but a nonspecific periostitis had to be assumed in the other 2 cases.

In the fourth case a complete syndrome of the sphenoid fissure developed during the progress of an intracranial new growth. The patient had no pain, and the onset was gradual, with the pathologic changes developing over a period of a year and a half. Through operation, the cause was found to be a basilar meningioma originating somewhere in the anterior fossa.

The main and earliest symptoms in the cases of the infectious type of syndrome were deep pain behind the eye, radiating to the forehead, temple and top of the head on the same side, and tenderness with pressure on the eyeball. Other symptoms in all cases were ptosis, complete ophthalmoplegia and slight exophthalmos, perceptible with the exophthalmometer only. Further symptoms were anesthesia or hypesthesia of the forehead, upper lid and cornea (cases 2 and 3), involvement of the optic nerve (cases 1 and 3) with secondary atrophy and a slight rise in temperature, to 99 to 99.4 degrees (case 3), the last pointing to an inflammatory process. A roentgenogram showed narrowing of the palpebral fissure on the involved side in case 1 and revealed no definite changes in case 2 and none in case 3. Specific therapy in the form of injections of tebeprotin (Toennisen) could be administered in case 2; in case 1 potassium iodide, aminopyrine and salicylates were given, and in case 3 typhoid vaccine was administered. Also in case 2 an exploratory intracranial operation was performed. In all 3 cases recovery occurred with full vision, although the same disease of the first eye in cases 1 and 3 ended in atrophy of the optic nerve.

REVIEW OF THE LITERATURE

The literature of this syndrome is not too scarce in French, in which language numerous theses have been written on the subject since 1895, the material usually being grouped under the various etiologic factors. Cases were reported previous to 1896, but during this year Rochon-Duvigneaud[1] first described the condition as a pathologic entity in which the symptoms and clinical findings were limited to this area under the term "sphenoid fissure syndrome." In his 3 cases the causative agent was syphilis and recovery followed the use of anti-

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1. Rochon-Duvigneaud, A.: Quelques cas de paralysie de tous les nerfs orbitaires (ophtalmoplégie totale avec amaurose et anesthésie dans le domaine de l'optalmique d'origine syphilitique), Arch. d'opht. **16**:746 (Dec.) 1896.

syphilitic therapy. Rollet[2] in 1865 had pointed out the production of ocular paralyses by syphilitic periostitis of the sphenoid fissure but had not considered this a clinical or pathologic entity.

From this time on, articles appeared in the French literature at infrequent intervals, the most thorough description originating from Dejeans in 1927,[3] in which all the reported cases were reviewed and a detailed bibliography was provided under the title of "Paralytic Syndromes of the Summit of the Orbit." The etiologic factors were considered by him to be: malignant tumors, primary or secondary; traumatism and infections, either specific or nonspecific. He stated that Dinkler[4] in 1891 reported the first case in which the syndrome was due to a tumor of the sphenoid bone and that later Berthaux collected all published cases and discussed them in his thesis. Dejeans contributed 2 more cases to this group. The first report of the syndrome due to traumatism was made by Badal and Fromaget[2] in 1894, according to Dejeans. Instances of the syndrome due to syphilis have been reported by Poulet,[2] Villemonte-Laclergerie,[5] Hutchinson Jr.,[2] Fromaget[6] and Landman.[7] Cases in which the syndrome was due to a nonspecific infection had been described by Worms, Terrien and Oswald.[2] Dejeans contributed 3 more cases to the infectious group, 1 syphilitic and 2 nonsyphilitic. Analyzing his own and other material, he expressed the belief that four types of this syndrome can be described as follows:

1. The syndrome is complete when all the nerves in this region are involved, including the optic nerve. There is complete ophthalmoplegia from involvement of the third, fourth and sixth cranial nerves and the sympathetic fibers; sensory and vasomotor disturbances in the distribution of the ophthalmic branch of the fifth cranial nerve and atrophy of the optic nerve.

2. When the pathologic process is limited to the sphenoid fissure, the optic nerve is spared. A complete ophthalmoplegia results with sensory and vasomotor disturbances from involvement of the ophthalmic branch of the fifth cranial nerve.

3. The paralysis could be limited to the extrinsic and intrinsic muscles of the eye with the trigeminal and optic nerves intact.

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2. Original article not available for study.

3. Dejeans, C.: Le syndrome paralytique du sommet de l'orbite, Arch. d'opht. 44:657 (Nov.) 1927.

4. Dinkler, cited by Dejeans.[3]

5. Villemonte Laclergerie, G. J. M.: Ophtalmoplégie sensitivo-motrice totale de l'oeil droit avec cécité, Arch. d'opht. 29:623, 1909.

6. Fromaget, C.: Névrite du nerf optique, du trijumeau et de la troisième paire guérie par le cyanure de mercure intra-veineux, Clin. opht. 31:90 (Feb.) 1927.

7. Landman, O.: A Case of Monocular Ophthalmoplegia Interna and Externa with Paralysis of the Abducens and Trochlear, Arch. Ophth. 36:367, 1907.

4. Finally, the paralysis could still be more limited and could, for example, involve only the third cranial nerve and parasympathetic fibers.

Roger and Alliez [8] in 1935 reviewed the literature to date to determine the causation of this syndrome. In all, they collected 50 cases, excluding those in which the syndrome was attributed to traumatism and sinus infection. The syndrome in 20 of these cases was due to neoplasm and in 16 to syphilis, as determined by the history and laboratory findings; in 11 the cause was undetermined. In a footnote the authors commented that it is a curious fact that a tuberculous origin was rarely reported by older authors and had not been found in any of their cases. They contributed 15 cases of their own to the group, in 7 of which a neoplasm was the contributing factor, cancer of the sphenoid in 2, metastatic tumors in 4 (breast, kidney, lung and intestine) and a disseminated epithelioma of unknown origin in 1. Among the other 8 cases, the patients' ages ranging from 30 to 72, there was only 1 case in which the syndrome would seem to be syphilitic in origin because of the Argyll Robertson pupil and absence of the achilles reflex; however the test of the blood was negative. In the other 7 cases the causation was uncertain. Antisyphilitic therapy ameliorated the condition occasionally in three to four weeks but usually in three to ten months. This led the authors to conclude that the condition was due to a peculiar form of occult syphilis at the summit of the orbit, and they urged mercury and bismuth therapy in all cases in which the causation is obscure.

In the British literature Tait [9] reported a typical case of this syndrome in a 17 year old girl in whom the Wassermann reaction was negative and the spinal fluid was normal in all respects. The condition was bilateral, with involvement of the left side coming on ten days after that on the right. The patient returned to normal after roentgen therapy and had no recurrences or changes indicative of an intracranial lesion in a four year period of observation. Tait called attention to the discussion of ocular palsies by Collier,[10] who pointed out the interesting group of peripheral palsies of the oculomotor nerves so frequently overlooked in teaching and textbooks, namely, the paralyses due to inflammatory lesions in the region of the sphenoid fissure which might involve the third, fourth and sixth cranial nerves, the first division of

8. Roger, H., and Alliez, J.: Etiologie des syndromes de la fente sphénoïdale et de l'apex orbitaire: Efficacité du traitement antisyphilitique, Rev. d'oto-neuro-opht. **13**:245 (April) 1935.

9. Tait, C. B. V.: Ophthalmoplegia Associated with Bony Changes in the Region of the Sphenoidal Fissure, Brit. J. Ophth. **18**:532 (Sept.) 1934.

10. Collier, J. S., in Discussion on Ocular Palsies, Proc. Roy. Soc. Med. (Sect. Neurol & Ophth.) **14**:10, 1921.

the fifth cranial nerve and possibly the optic nerve but never spread to the inner part of the orbit. He referred to these as orbital periostitis or fibrositis and stated that he had followed 40 cases of this type, with recovery in all. The nonsyphilitic nature of the condition is stressed, since only in 1 case in this group was there a positive Wassermann reaction, and Collier pointed out what seemed to be a close analogy between this condition and the common paralysis of the peripheral portion of the facial nerve, or Bell's palsy, as regards symptoms, causation and recovery. The incidence in his series was from puberty to old age but was most common in the first half of adult life. The characteristic symptoms were described as orbital pain, neuralgic in character, spreading over the same side of the head; slight but always detectable proptosis; tenderness with pressure on the globe; ocular paralyses and loss of sensibility in the distribution of the ophthalmic branch of the fifth cranial nerve. In 2 of the cases it was obvious that the sixth cranial nerve was recovering, while the nerves at the inner angle of the sphenoid fissure were becoming involved. In a few of the cases the condition was bilateral, and in 1 the interval between the involvement of each side was nine years. The fact was stressed that malignant involvement of this region does not give a clearcut picture of the syndrome.

In the American ophthalmologic literature a typical case of sphenoid fissure syndrome due to a syphilitic infection was reported by Hunter [11] in 1900 under another title and was considered to be due to a gumma at the apex of the orbit which melted away with antisyphilitic therapy. The optic nerve was involved, resulting in impaired vision, but all motor nerves recovered. Landman [7] described a similar case in which the optic nerve was spared. He brought out the fact that when the ophthalmoplegia is at its height the severe neuralgia pain has subsided, as illustrated in case 3 of this report. In writing on this subject Duane has said: "Paralyses of the first branch of the fifth (with perhaps keratitis paralytica) combined with paralyses of the third and optic nerve atrophy indicate disease (syphilitic periostitis) in the sphenoidal fissure." [12]

In the American nonophthalmologic literature Finlay,[13] of Habana, Cuba, reported under the title of sphenoid fissure syndrome 2 typical cases in which the syndrome was due to syphilitic lesions situated at

11. Hunter, D. W.: A Case of Gumma of the Apex of the Orbit, New York Eye & Ear Infirm., Rep. **7:**17 (Dec. 17) 1900.

12. Duane, A.: The Extraocular Muscles, in Posey, W. C., and Spiller, W. G.: The Eye and Nervous System, Philadelphia, J. B. Lippincott Company, 1906, chap. 5.

13. Finlay, O. E.: Two Cases of Syphilitic Lesions Situated at the Sphenoidal Fissure: Sphenoidal Fissure Syndrome, South. M. J. **23:**51 (Jan.) 1930.

the sphenoid fissure. Recovery without involvement of the optic nerve followed the administration of antisyphilitic therapy. He reviewed the literature, stressing principally Dejean's discussion of the subject. Jackson [14] presented a case of unilateral ophthalmoplegia totalis which would seem, from the material given, to be a typical instance of this syndrome due to infection but which he considered to be a phase in an attack of epidemic encephalitis. Sufficient data are not given to interpret the facts. Ré and Muhlmann [15] in the South American literature described a case of this syndrome due to syphilis in which the symptoms, clinical findings and progress are classic. Probably there are other cases published but hidden under another diagnosis or as a part of a more extended symptom complex.

All authors stressed the point that in cases in which the syndrome is due to trauma the onset is sudden and irregular and that symptoms vary, depending on the site of the bony lesion when present and on the amount and localization of the extravasated blood. Only if the integrity of the nerves is maintained does recovery occur and the symptoms disappear. A recent case report by Venco [16] illustrates these points well.

In cases of tumor the symptoms are irregular and slowly progressive, and the clinical manifestations are complicated, being dependent on the extension of the tumor into the orbit, cranial cavity or both. Herzau [17] reported 8 cases of tumor in the region of the sphenoid fissure, in none of which was a typical sphenoid fissure syndrome present. David and Hartman,[18] in reviewing 26 cases of tumor of the lesser wing of the sphenoid bone from their own practice, stated that much to their surprise they did not find a single instance of a complete and typical syndrome of the sphenoid fissure.

SUMMARY

Three cases are herewith presented, 2 of orbital apex–sphenoid fissure syndrome and 1 of purely sphenoid fissure syndrome due to infection.

14. Jackson, J. DeW.: Unilateral Ophthalmoplegia Totalis Probably Due to Encephalitis Lethargica, Pennsylvania M. J. **33**:161 (Dec.) 1929.

15. Ré, B. V., and Muhlmann, V.: Sindrome de la hendidura esfenoidal curado, Semana méd. **2**:240 (July 27) 1933.

16. Venco, L.: Sopra una sindrome incompleta dell' apice orbitario di origine traumatica, Riv. oto-neuro-oftal. **14**:20, 1937.

17. Herzau, W.: Zur Klinik der ein-und doppelseitigen Ophthalmoplegien peripheren Ursprungs, Arch. f. Ophth. **125**:207, 1930.

18. David, M., and Hartman, E.: Les symptômes oculaires dans les méningiomes de la petite aile du sphénoïde, Ann. d'ocul. **172**:177 (March) 1935.

The first, or complete, syndrome involves the second, third and fourth cranial nerves, the first division of the fifth and sixth cranial nerves and sympathetic fibers.

The second, or incomplete, syndrome spares the optic nerve.

A fourth case is described in which the complete syndrome was produced during the development of an intracranial tumor.

It is important to make the correct diagnosis early, because of the danger to the optic nerve through compression, and it is likewise important to distinguish between an infectious process and a new growth, so that the patient is not unnecessarily submitted to an intracranial operation.

UNUSUAL CHANGES IN THE RETINAL VEINS IN DIABETES

C. S. O'BRIEN, M.D.

AND

J. H. ALLEN, M.D.

IOWA CITY

Retinal varices are rarely observed but may be seen occasionally in association with the vascular changes which occur in the retinitis of diabetes. Sclerosis of the retinal vessels is an almost constant finding in adults who have had diabetes over a period of years. Probably such changes in the vascular system are either hastened or even brought about in some way by the metabolic disturbances associated with the disease. The retinitis of diabetes is believed to be the result of such pathologic alterations in the vascular system.

Ophthalmoscopic examinations of several hundred diabetic patients, over a period of years, revealed many with the typical signs of retinitis. Almost invariably sclerosis of the retinal vessels was in evidence, and in an occasional case varices of the retinal veins were noted. Further observations showed that these venous changes occurred almost exclusively in patients with diabetes and arteriosclerosis, but occasionally they were present in those with arteriosclerosis alone. Most frequently the varices were found in those with poorly controlled, long-standing diabetes.

Only rarely in the literature has any mention been made of varices along the retinal veins. In 1883 Story and Benson [1] reported their observations on a 20 year old man with aneurysms of the arteries and veins of the retina, but no mention was made of diabetes or arteriosclerosis. Nettleship,[2] in a case reported in 1888, mentioned for the first time varices of the retinal veins in the fundus of a diabetic subject.

1. Story, J. B., and Benson, A. H.: Aneurysms on Retinal Vessels in a Peculiar Case of Retinitis, Tr. Ophth. Soc. U. Kingdom 3:108, 1883.

2. Nettleship, E.: Haemorrhagic Retinitis in a Patient with Diabetes: Varicose Swellings on a Retinal Vein in the Right Eye, Tr. Ophth. Soc. U. Kingdom 8:161, 1888.

Raehlmann [3] in 1889 reported a case of arteriosclerosis with variations in the caliber of the retinal veins and stated that they also occurred in a young adult with syphilis and in a case of tumor of the brain associated with postpapillitic atrophy. Dimmer [4] in a text published in 1921 mentioned that varices of the retinal veins are also seen occasionally in cases of hemorrhagic retinitis and in leukemic fundi. Manolescu [5] reported variations in the caliber of the retinal veins in a case of hyper-
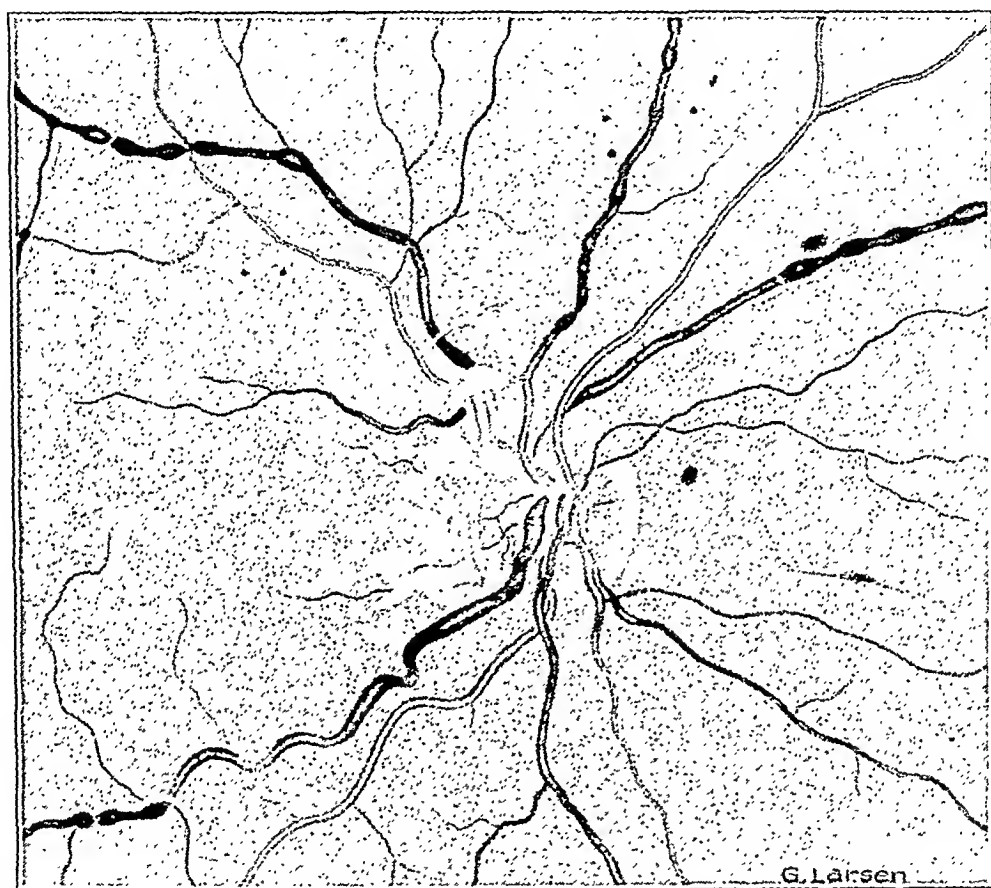
Fig. 1.—Varices and sclerosis of the retinal vessels; also multiple hemorrhages, cytoid degeneration and proliferating retinitis.

tensive disease. In 1931 Gray [6] described 4 cases of diabetes in which the retinal veins had a somewhat beaded appearance. Bonnett and

3. Raehlmann, E.: Ueber miliäre Aneurysmen an den Netzhautgefässen und Netzhautblutungen, Klin. Monatsbl. f. Augenh. 27:241, 1889.

4. Dimmer, F.: Der Augenspiegel, Leipzig, Franz Deuticke, 1921.

5. Manolescu: Allgemeine Arteriosclerose und Varisen der Retinalvenen, Zentralbl. f. d. ges. Ophth. 12:128, 1924.

6. Gray, W. A.: Retinal Vessel Changes in Diabetes, Tr. Ophth. Soc. U. Kingdom 51:108, 1931.

Bonamour [7] in 1938 described 3 cases of retinitis of hypertensive disease and diabetes in which varices were observed.

As has been stated, varicosities of the retinal veins are rare and apparently occur almost exclusively in adults with poorly controlled diabetes and arteriosclerosis. Herein is a report of 21 cases of diabetes with retinitis and retinal varices.
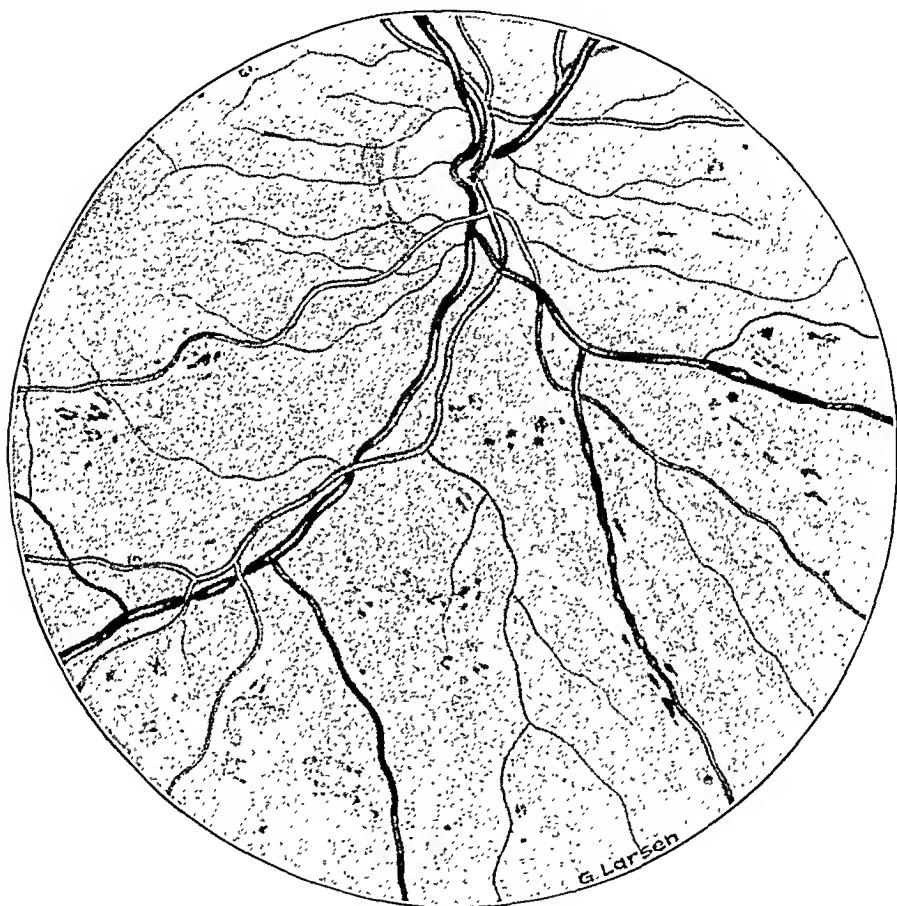
Fig. 2.—Varices of the inferior nasal branch of the central retinal vein, arteriosclerosis and retinitis.

In this group of cases 13 of the patients were women and 8 were men, ranging in age from 36 to 65 years. Symptoms of diabetes had been present over a period of two to twenty-five years, with an average of ten years. In every case control of the diabetes had been poor, and on the patient's admission the blood sugar ranged from 179 to 447

7. Bonnett, P., and Bonamour, G.: Les altérations des vaisseaux de la rétine observées à l'ophtalmoscope dans le diabète compliqué d'hypertension artérielle, Bull. Soc. d'opht. de Paris **50**:367, 1938.

mg. per hundred cubic centimeters, with an average of 305 mg. On admission sugar was present in the urine of 14 patients, while that of 7 showed none; there was albumin in the urine of 15 patients, casts in that of 4 and some diacetic acid in that of 2. The systolic blood pressure ranged from 108 to 240 mm. of mercury and the diastolic pressure from 65 to 110 mm., with an average systolic pressure of 170 mm. and an average diastolic pressure of 92 mm. On physical exami-
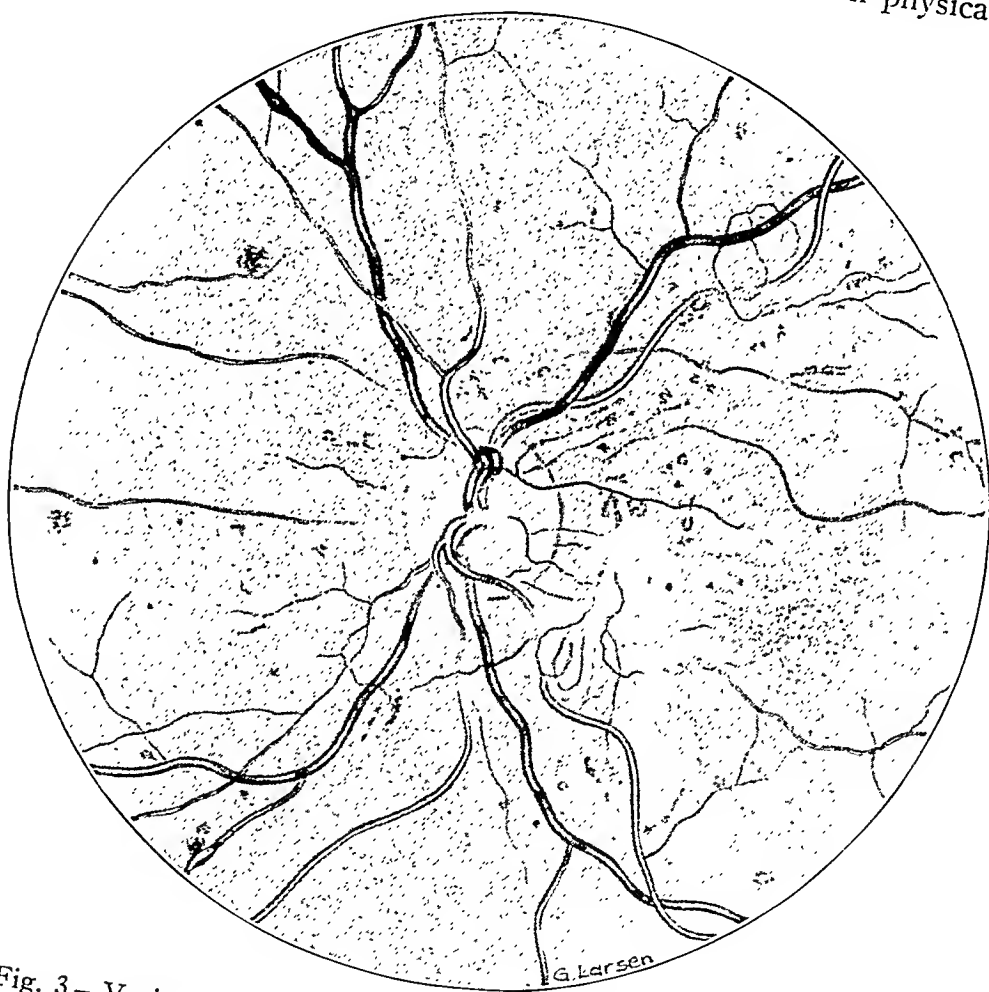
Fig. 3.—Varix of a branch of the inferior nasal vein; also retinitis.

nation 19 of the 21 patients were found to have generalized arterio-sclerosis and 5 showed nephrosclerosis, the latter diagnosis having been based on the presence of generalized arteriosclerosis and dimin-ished renal function. Nine patients had enlargement of the heart and 5 coronary disease. Seven patients had gangrene of one or both feet, 1 had ulcers, 2 had spots of brownish discoloration on the legs or feet and 3 showed edema of the lower extremities. In 4 of the patients with gangrene and in 2 others who showed no gangrene there was

diminished sensation. Other complicating conditions were encountered, but these had no relation to the ocular findings.

Vision was diminished in 16 patients. In every case the retinal vessels were sclerosed and hemorrhages were seen in the retina; in all but 1, small sharply marginated, yellowish white areas of retinal degeneration were present. Woolly areas of cytoid degeneration were observed in 15 patients. Evidences of proliferating retinitis were seen

Fig. 4.—Varices and sclerosis of the retinal vessels, diabetic retinitis and venous thrombosis.

in one or both eyes of 9 patients, and hemorrhages in the vitreous were present at one time or another in 3 patients.

All of these patients showed varicosities of the retinal veins (figs. 1 to 6). The varices were observed most frequently in the larger veins; they appeared not to have any relation to arteriovenous crossings, since they were located at some distance both distal and proximal to points where arteries and veins crossed. In some eyes the varices

alone gave evidence of venous changes, but in others a white line along either side of the vessel gave proof of sclerosis. Venous engorgement was noted occasionally. Frequently the affected vein showed constrictions of the lumen alternating with varices, thus giving an exaggerated beaded or sausage-like appearance. In 5 cases venous thrombosis was present in either the central vein or one of its branches. Certainly sooner or later thromboses must occur with more or less regularity in such vessels.
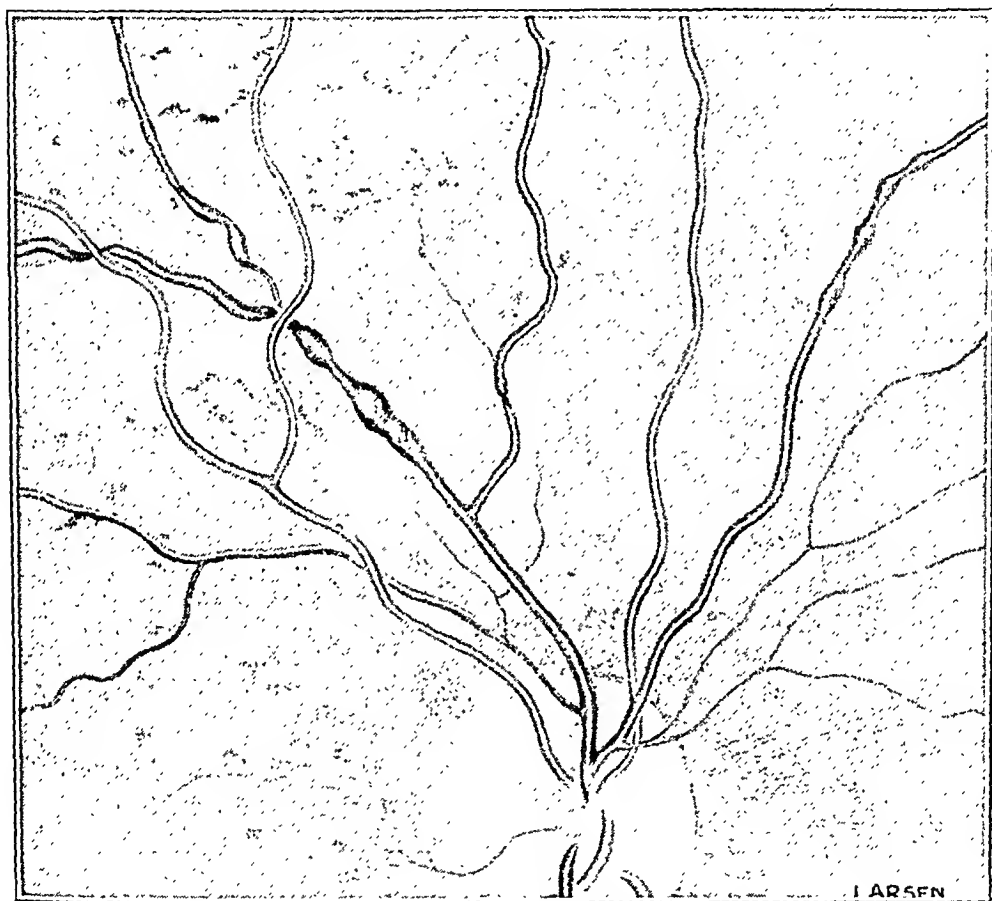
Fig. 5.—Appearance of the fundus one year before removal of the eyeball. Varices, arteriosclerosis and diabetic retinitis are present.

An eye with secondary glaucoma removed from one of these patients was available for microscopic study (figs. 5 and 6). The patient, a man aged 65, had been diabetic for fifteen years, during which time the disease had been poorly controlled. On his admission to the hospital the blood sugar was 447 mg. per hundred cubic centimeters, the blood pressure was 170 systolic and 110 diastolic and physical examination revealed generalized arteriosclerosis with vari-

cose veins in the extremities. There was a typical retinitis, with arteriosclerotic changes in the retina and many varices of the retinal veins. Microscopic examination of serial sections revealed advanced pathologic involvement of the retinal vessels. There was pronounced sclerosis of the arteries and arterioles, as evidenced by the thickening of the medial and inner coats (figs. 7 and 8). The walls in many areas had undergone hyaline degeneration, and endothelial proliferation had pro-
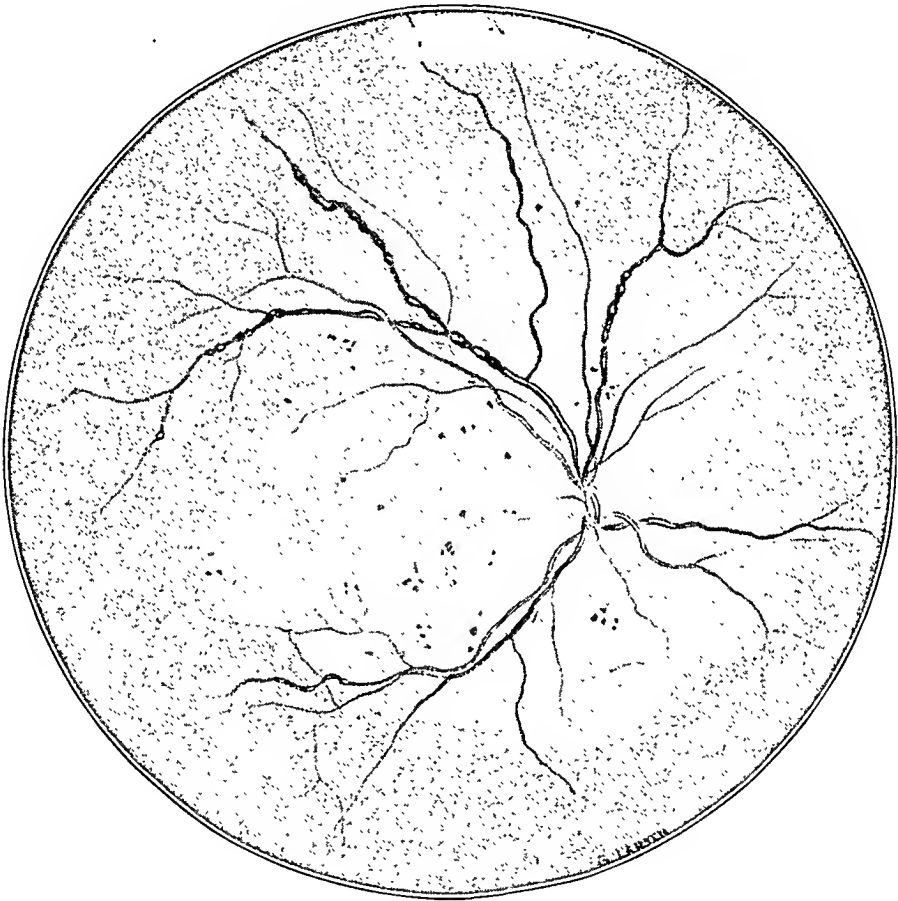
Fig. 6.—Drawing of the posterior segment made under a dissection microscope after removal of the eyeball and fixation in a solution of formaldehyde.

duced an endarteritis obliterans in a number of the smaller vessels (figs. 9, 10 and 11). The veins were sclerosed, and the walls showed slight variations in thickness; they did not appear to be thicker at the arteriovenous crossings than elsewhere (figs. 12 and 13). In places the walls had undergone hyaline degeneration. Endothelial proliferation was present in many areas, and thromboses were common. In

the region of the varices the veins were unevenly dilated and the walls were sclerosed and thickened rather than thinned, as one might expect (figs. 14 and 15). Many hemorrhages were encountered in the retina, and areas of degeneration were seen in the internuclear layer.

Fig. 7.—Advanced sclerosis of a retinal arteriole.

SUMMARY

Varices of the retina are uncommon but are seen occasionally in patients with the retinitis of diabetes and more rarely in those with arteriosclerotic retinitis. In addition to the typical findings of diabetic retinitis with its commonly associated arteriosclerotic changes, the veins show irregular, localized varicosities. Under the microscope the veins appear sclerosed, the wall showing variations in thickness, hyaline degeneration, endothelial proliferation and thromboses.
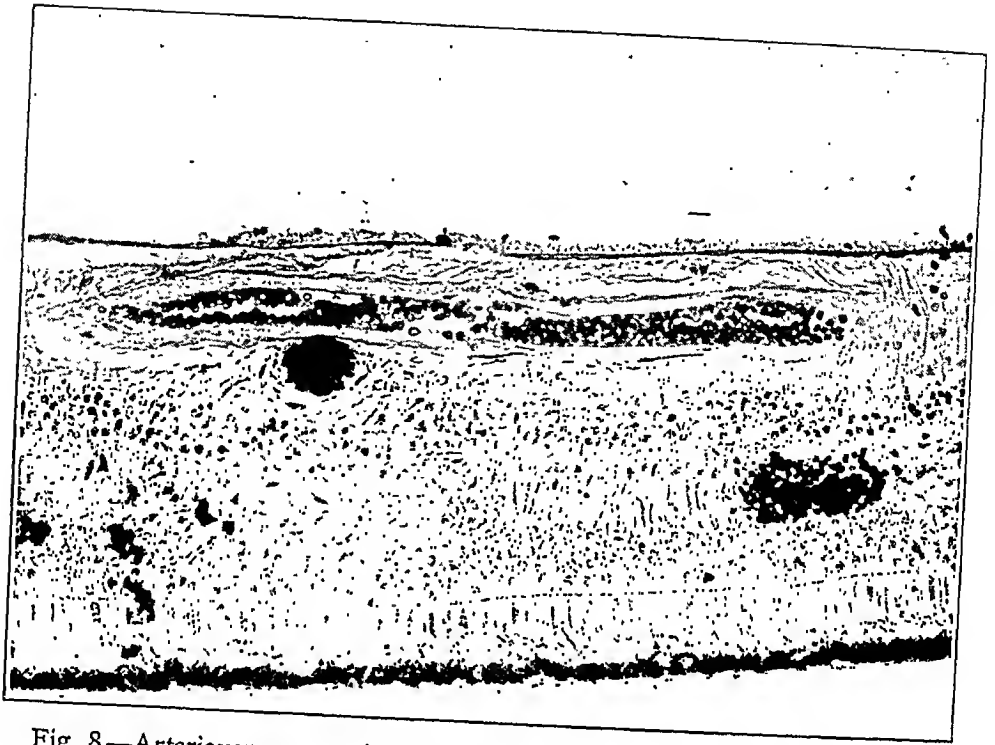
Fig. 8.—Arteriovenous crossing; advanced sclerosis of a small artery (in longitudinal section) and thickening of the walls of the underlying vein; hemorrhages and areas of degeneration in the retina.
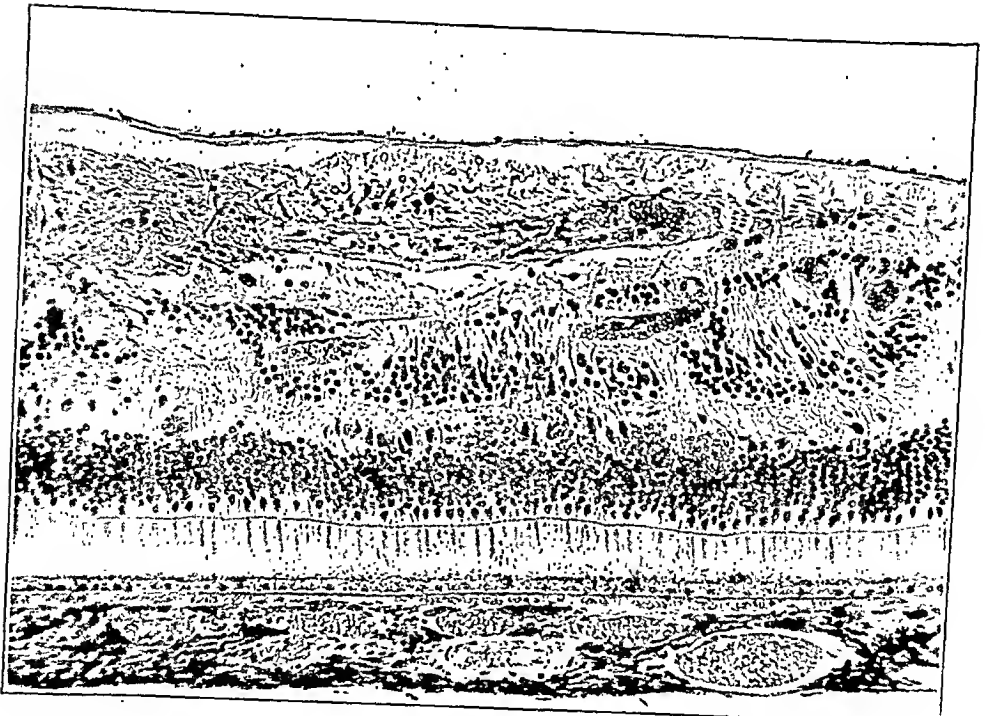
Fig. 9.—Endothelial proliferation with thrombus formation in a small artery.
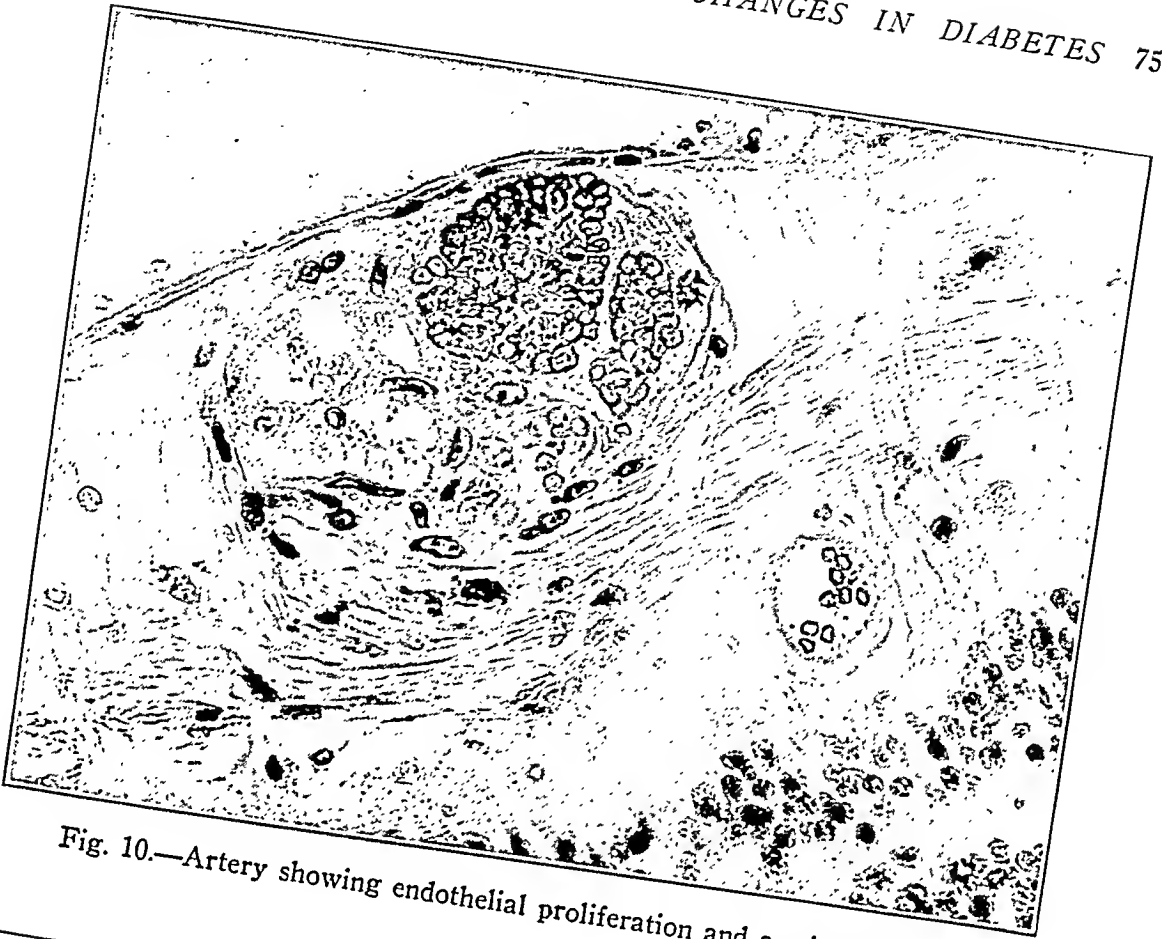
Fig. 10.—Artery showing endothelial proliferation and a mitotic figure.
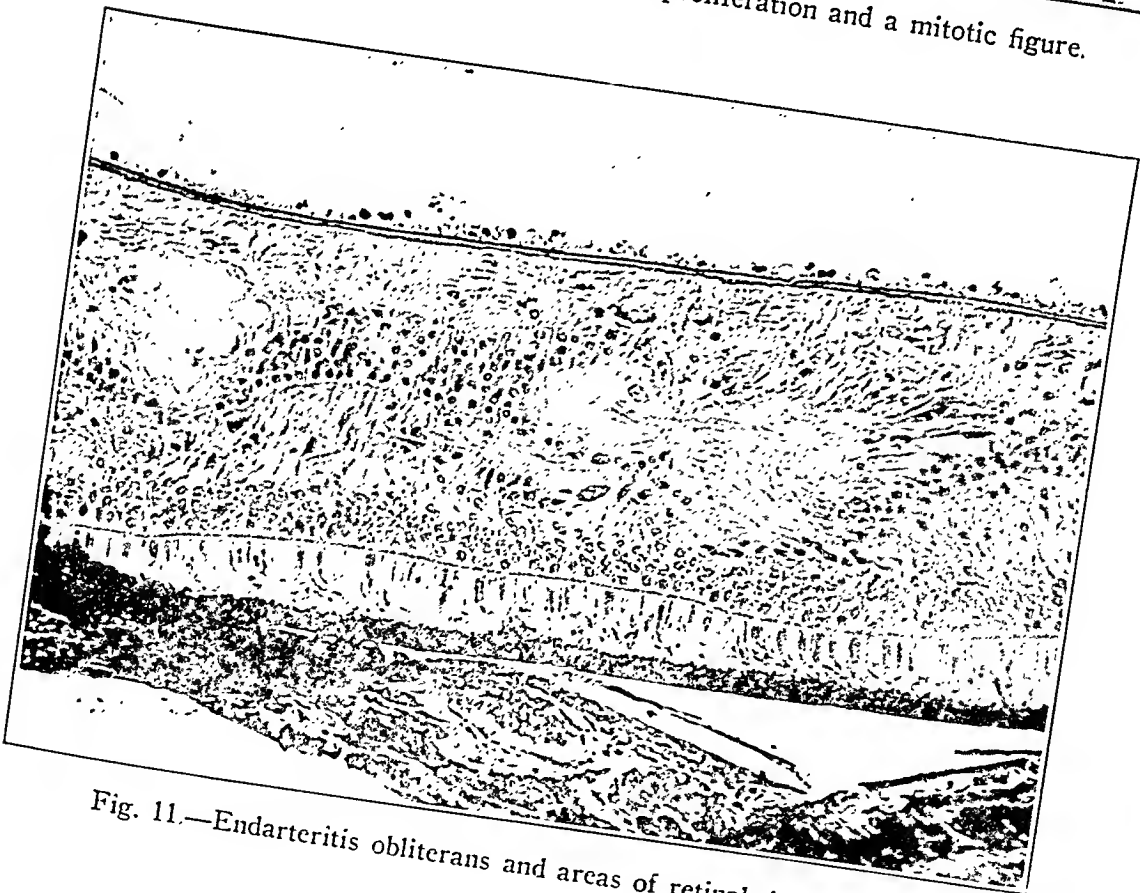
Fig. 11.—Endarteritis obliterans and areas of retinal degeneration.
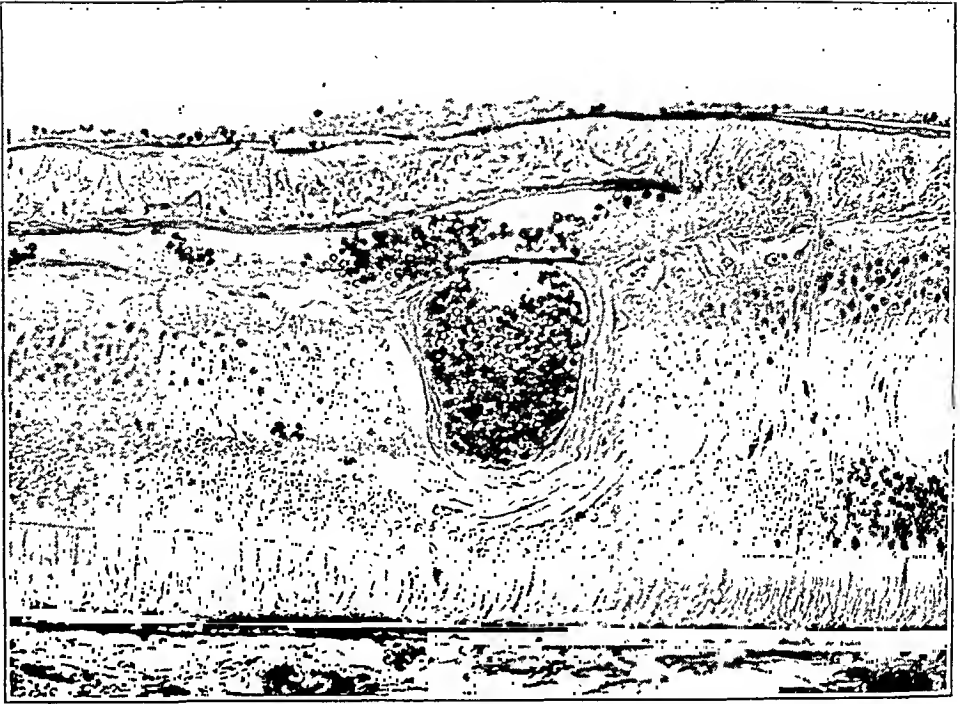
Fig. 12.—Sclerosis of a large vein at an arteriovenous crossing.
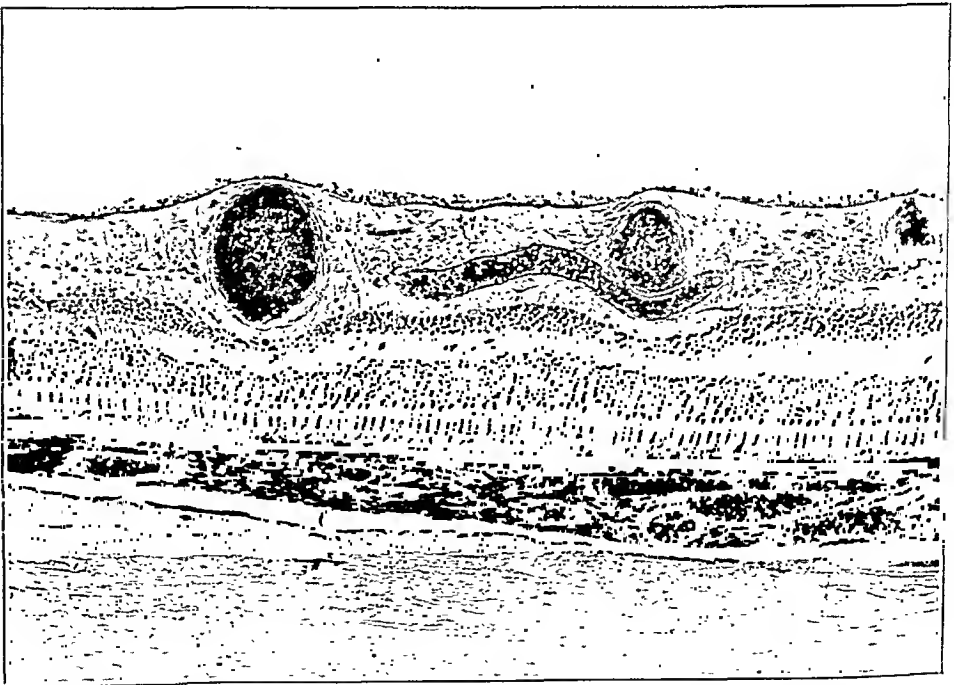
Fig. 13.—Arteriovenous crossing showing the vein rounding a sclerosed artery;
mild, if any, sclerosis of the vein.
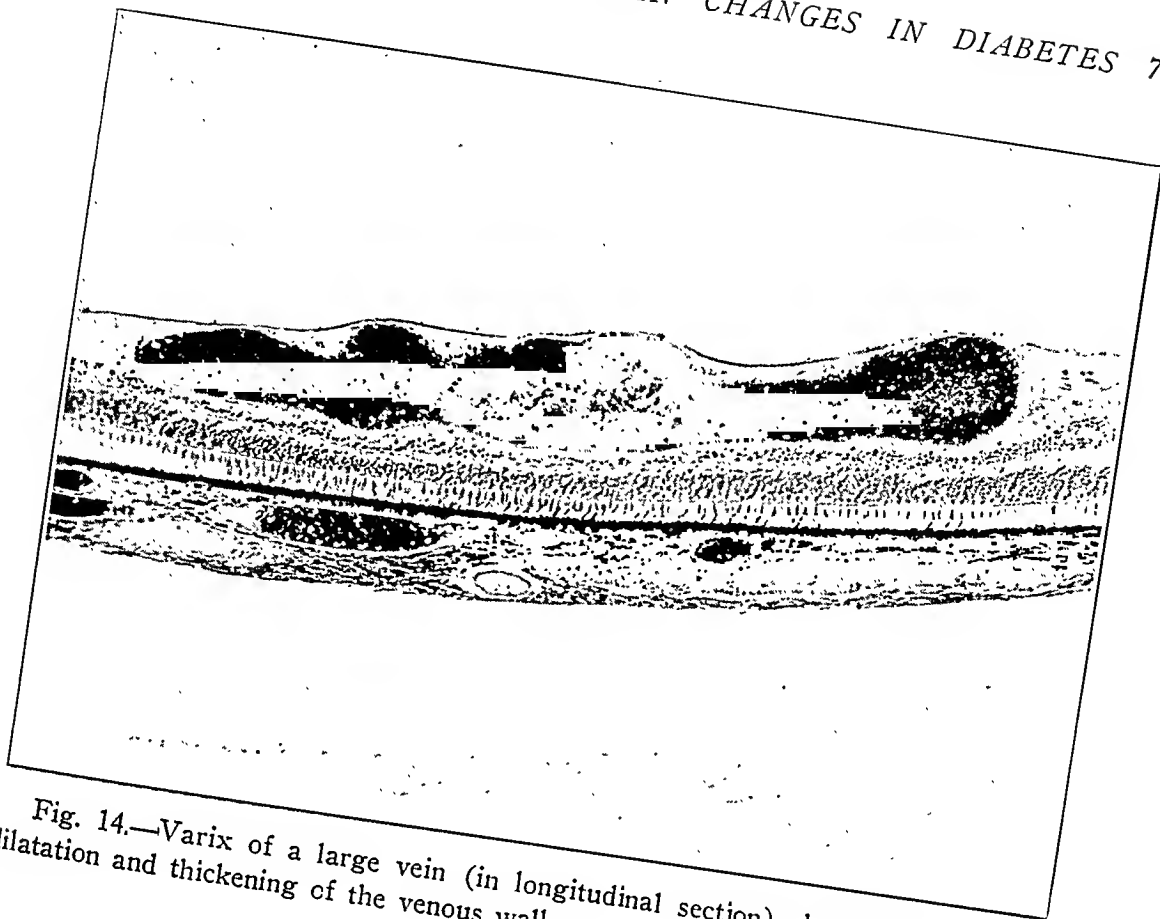
Fig. 14.—Varix of a large vein (in longitudinal section) showing the uneven dilatation and thickening of the venous walls.
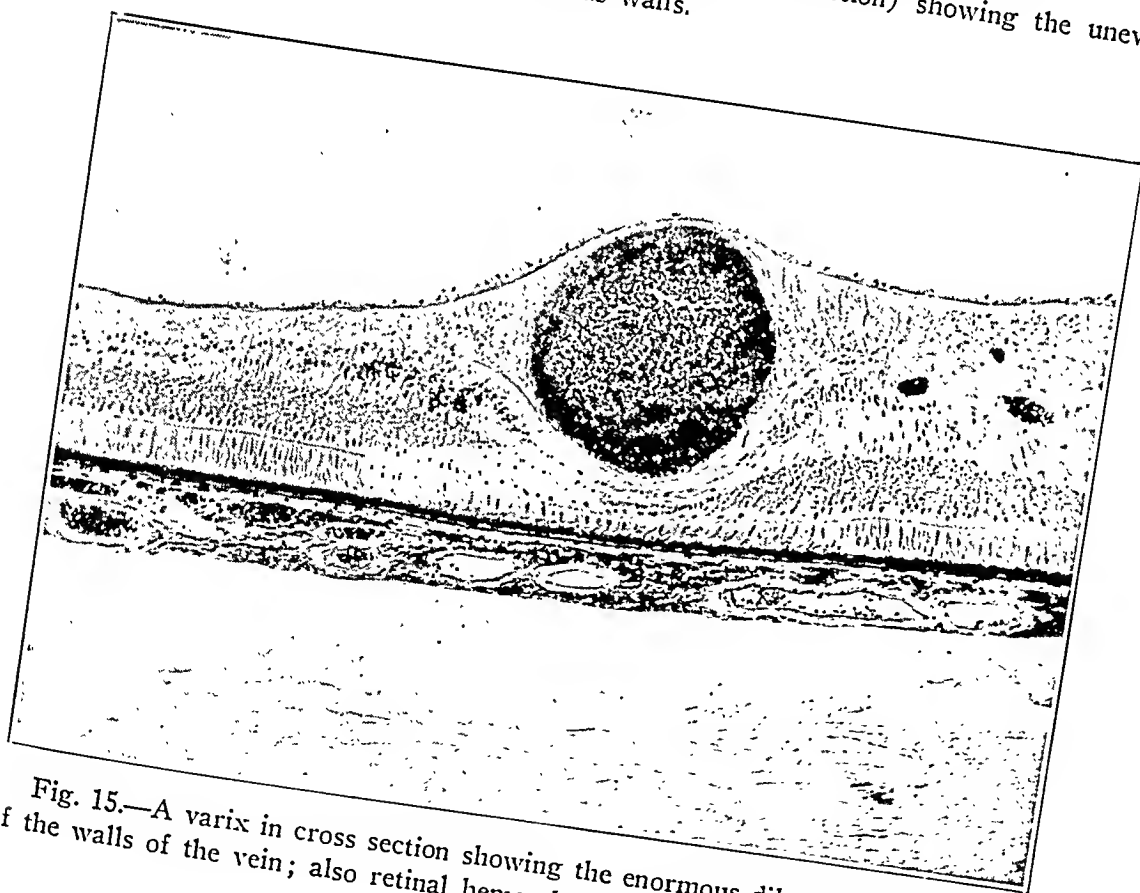
Fig. 15.—A varix in cross section showing the enormous dilatation and sclerosis of the walls of the vein; also retinal hemorrhage and degeneration.

ABSTRACT OF DISCUSSION

Dr. Parker Heath, Detroit: The first description of retinal changes in diabetes as observed ophthalmoscopically was published in 1856 by Jaeger. Nettleship in 1887 enlarged the literature about the objective findings of this relation. Hirschberg in 1890 classified the retinal picture thus: (1) exudative forms with punctate central retinitis; (2) hemorrhagic forms, and (3) exaggerated inflammatory signs, usually with renal disease associated.

Since then relatively little has been added except descriptive matter and some refinements.

This is true because diabetic retinitis is a local manifestation in a highly differentiated tissue of a general metabolic disease of obscure etiology. Furthermore, reports of histologic studies are scanty. Some authors have stated that diabetes is not a cause of the retinitis; others prefer the names retinography and retinosis, implying no inflammation.

The morphologic picture presented by Hanum in 1938 very well groups the objective signs thus:

1. The exudative type
   (*a*) exudative diabetic retinitis, composing 60 per cent of the cases
   (*b*) circinoid diabetic retinitis, composing 9 per cent
2. The hemorrhagic type
   (*a*) hemorrhagic diabetic retinitis, comprising 25 per cent
   (*b*) proliferative diabetic retinitis, comprising 12 per cent

The average ophthalmologist sees these patients with or without elaborate classifications and decides from impressions that the cause is probably diabetic. And what are these impressions? First, the veins are darker in color. Second, the disease is usually confined to the posterior part of the globe; it is characterized by exudates in two forms: a dotlike, angular, small fibrotic form or the very larger fat type. The latter are rather rare.

The startling thing about the punctate hemorrhages is that some dots disappear rapidly; others stay in the same place for several weeks. Why the change occurs in one place and not in the other is obscure.

The main difficulties for the ophthalmologist lie with the complications of diabetic retinitis, namely: albuminuria, glycosuria, vascular sclerosis and hypertension. These really present difficulties in differential diagnosis.

The authors described the sign of varices of the retinal veins found in diabetic retinitis. Their description is supported by a study of pathologic material from 1 patient. To differentiate the condition in this case from vascular sclerosis, putting it into the diabetic group, is difficult. The walls of the vessels are sclerosed and show hyaline degeneration. The lumen may be plugged by endothelial proliferation. The caliber of veins is markedly irregular.

There are few reports of histologic studies in the literature. The two principal ones are those of Beenovieux and Pesme (1923), who found degeneration of the nerve elements as well as vascular changes above, and of Koyomagi (1935), who found no sclerotic changes in his case. He noted sclerosis only in the small vessels in the inner granular layer and also degenerative changes in the ganglion cell layer.

A need thus exists for the study of more tissue. The writers ably presented their series of cases. A larger series with less evidence of sclerosis will give information of more value. The percental frequency of varices of the veins is important. The joint findings of the percental frequency and more histologic studies will substantiate or disprove the permanent importance of the essayists' findings.

Dr. EDWARD R. THOMAS, Dayton, Ohio: In this paper there are several factors for discussion. First, there are the varices of retinal veins which have been described as an infrequent occurrence in diabetic patients in whom the disease has been present and uncontrolled over a long period, or do they represent incidental findings in a few patients in a large group, with other factors predisposing to the formation of varices? In this group of patients many had symptoms and signs of cardiovascular and renal arteriosclerosis, as manifested by myocardial disease, nephrosclerosis and gangrene.

I reported recently the observations on 48 patients with diabetic retinitis. In this group were several patients with renal complications, hypertension and arteriosclerosis who exhibited dilated and tortuous retinal veins, but in none did I observe isolated varices along the retinal veins. In viewing these dilated and tortuous veins, portions of the veins arched above the retinal layers, and portions of the vessel remaining in the retina were partially hidden by edematous areas. When viewed by the ophthalmoscope, there was a foreshortening of parts of the vessel, producing the picture of pseudovarices along its course.

The predisposing factors of varices are congenital defects of the structure of the wall of the vein and obstruction of the lumen of the vessel, in which continued pressure from the blood column results in dilatation and tortuosity of the vessel.

With sclerosis of the vessels as a predisposing factor, partial or total thrombosis of the vein may be a primary cause of the varix. If such thrombi accompany diabetes, some toxic metabolic substance carried in the blood would be the etiologic factor. If this is true, varices should be generalized.

In the patients described by Drs. O'Brien and Allen the varices were not generalized but were confined to individual branches and were usually somewhat distant from the central vessels.

If the cerebral vessels, which have a common origin with the retinal vessels, may be used as a criterion of the frequency of retinal arteriosclerosis in patients with diabetes, there is a striking absence of reports of any such relation. Root, Sharkey and Warren stated that the arteriosclerosis commonly seen in diabetic patients is of the atheromatous type and is confined to the larger and medium-sized arteries throughout the body. Autopsies on 175 diabetic patients studied by Root and Sharkey showed that cerebral arteriosclerosis was no more frequently a cause of death in diabetic than in nondiabetic patients. Warren reported that 484 autopsies revealed that 76 per cent of the patients died of arteriosclerotic complications of the heart and lower extremities and only 12 per cent died of cerebral arteriosclerosis. Waite and Beetham stated that by direct examination of the fundi sclerosis of the retinal vessels was no more frequently observed in diabetic than in nondiabetic

patients. Hanum stated: "I have never found any relationship between the arteriosclerotic vascular changes and the gravity of the retinal changes."

This paper should arouse curiosity and stimulate careful observation of the retinal vessels of diabetic patients. If a significant instance of retinal varices is observed in such patients, such observations should certainly be reported.

Dr. ARTHUR J. BEDELL, Albany, N. Y.: In a discussion before the Academy of Ophthalmology and Otolaryngology last fall, I reported on yellow spots and retinal hemorrhages. The critical inspection of fundi and photographs continues. When the title was announced I rechecked photographs of the fundi of about 300 patients known to be suffering from diabetes.

Aneurysm-like dilatations were rare, and arteriolar sclerosis, as judged from the usually accepted standards, was found in less than 50 per cent of the cases.

Changes in the retinal veins have been given more and more prominence during the past years. Alterations suggesting congenital malformations have been observed, and, as the authors state, gross hemorrhages of the vitreous are not uncommon. A few photographs illustrate the locations of the extravasations, and several show results of retinitis proliferans. The proliferation seems to be the same as that following tuberculosis, hypertension and arteriosclerosis, for neither in location nor gross structure does it differ.

The authors have drawn attention to the necessity of correlating fundus signs and laboratory findings as well as confirm our impression of the serious nature of the venous changes in those suffering from diabetes.

I wish the authors would tell if they have any theory as to why some patients have hemorrhages and why others with seemingly identical conditions are free from them.

I feel that the term diabetic retinitis should not be used, because exactly the same fundus appearance is seen in patients without hyperglycemia.

Dr. JAMES H. ALLEN, Iowa City: The discussers have called attention to several interesting points and have given me the opportunity to emphasize the fact that we were not describing these changes as being typical of diabetes. In each of these patients we felt that there was a definite arteriosclerotic factor.

We agree with the objection to the term retinitis of diabetes and believe that such a term as retinosis is better.

We are not certain about the etiology of the so-called retinitis in diabetes, and we believe that it will require further clinical, pathologic and experimental observations to tell us many of the things that we should like to know.

In regard to the occurrence of varices in the retinal vessels, this condition was observed in considerably less than 1 per cent of patients with diabetic retinitis; consequently, I should like to emphasize the fact that it is extremely rare. We are fortunate in being able to see a large number of diabetic patients.

I might add that these patients have been followed over a period of several years. Only 1 in the series was seen but one time. That patient came in with gangrene of the extremities and died of secondary infection after a few days, but he had well developed varices in the retinal vessels.

We thought at one time that there might be some correlation between varices of the lower extremities and varices in the retinal veins, but the percentage of patients with varices in the lower extremities was small.

In reply to Dr. Bedell's question, we do not know why hemorrhages should occur in some patients and not in others. The 3 patients who had hemorrhages in the vitreous had these hemorrhages during our period of observation, and at a time when we felt the disease was well controlled. Perhaps the investigations of Dr. Dragstedt, of Chicago, on lipocaic may throw some light on this subject.

OCULAR PHARMACOLOGY OF FURFURYL TRIMETHYL AMMONIUM IODIDE

WITH SPECIAL REFERENCE TO INTRAOCULAR TENSION

ABRAHAM MYERSON, M.D.

AND

WILLIAM THAU, M.D.

BOSTON

Furfuryl trimethyl ammonium iodide is a new parasympathetic drug, having the following structural formula:
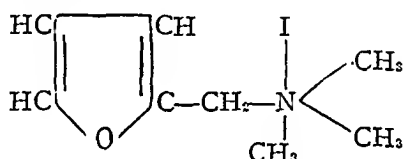
The animal pharmacology was developed by Fellows and Livingston,[1] who introduced the drug. They found that the drug is very stable in blood and produces a marked fall in blood pressure, cardiac inhibition and depression, an increased flow of saliva and an increased tone of intestine and bladder. These effects were overcome by atropine.

Myerson, Rinkel, Loman and Dameshek[2] have contributed the first paper on its pharmacology in man. The drug is effective by mouth in doses of from 5 to 20 mg. By intramuscular injection, 1 to 5 mg. will produce the full physiologic effects. These are, in general, similar to those produced by acetylbetamethylcholine (mecholyl chloride; mecholyl bromide), although differing in certain important respects. There are marked flushing, sweating and a drop in temperature which is probably the result of the sweating; the salivary flow is increased; the heart rate is elevated; the blood pressure is only slightly affected. There is increased peristalsis of the genitourinary and gastrointestinal tracts. The effects last about one hour and wear off gradually. All the effects

1. Fellows, E. J., and Livingston, A. E.: The Pharmacology of Certain Furfuryl and Tetrahydro-Furfuryl Ammonium Iodides, J. Pharmacol. & Exper. Therap. **68**:231, 1940.

2. Myerson, A.; Rinkel, M.; Loman, J., and Dameshek, W.: The Effect of Furfuryl Trimethyl Ammonium Iodide on Various Autonomic Functions in Man, J. Pharmacol. & Exper. Therap. **68**:476, 1940.

can be prevented by adequate doses of atropine, and similarly they may be stopped by adequate doses of the same drug, in this resembling acetylbetamethylcholine and other parasympathetic drugs. Furfuryl trimethyl ammonium iodide differs from acetylbetamethylcholine and other drugs in that it has no particular synergism with prostigmine, which is probably due to the fact that the cholinesterases have no effect on its chemical structure.

OCULAR PHARMACOLOGY

Instilled into the eye in a solution of from 5 to 20 per cent, preferably 10 per cent, the effects are prompt and marked, in every way similar to those of acetylbetamethylcholine, prostigmine, pilocarpine and the other well known parasympathetic drugs. The effects of furfuryl trimethyl ammonium iodide appear more promptly, are greater, last longer and are marked by one sign peculiar to itself and found in no other parasympathetic drug or other means of reducing intraocular tension, and that is it produces a narrow chamber while reducing the tension. Although this seems paradoxic, since every other para-sympathetic drug deepens the chamber, this effect of furfuryl trimethyl ammonium iodide is striking because the chamber appears so narrow as to seem nonexistent. On closer examination it is noted that only the center of the lens is projected forward as a result of increased accommodation, and this pushes the central and paracentral part of the iris forward, while the peripheral part, that is, the angle of the iris, remains wide. This effect was marked in the present series of subjects, while in a case of ocular pathologic involvement to be reported later the effect was reversed; that is, the chamber became deepened.

The usual parasympathetic effects appear. The palpebral fissure becomes narrowed, although not to the same extent as is seen with acetylbetamethylcholine. The pupil begins to contract in from two to four minutes, reaching maximal miosis, that is, 1 mm. or pinpoint size, in from five to seven minutes. The intraocular tension, with which we are especially concerned, begins to drop in from eight to ten minutes, reaching its maximum in about one hour.

These effects have been studied for several months, first, on animals (rats, guinea pigs and rabbits) and then on 20 subjects who were free of ocular pathologic involvement and, in the main, young patients with dementia praecox whose reactions to other drugs we have studied over a long period.

The intraocular tension, taken by the Schiötz tonometer for the group of subjects studied, prior to the instillation of the drug varied from 16 to 30. The drop in intraocular tension after fifteen to thirty minutes ranged from 3 to 7. This drop in intraocular tension lasted about

twenty-four hours, in some instances less—about twelve hours—and in others somewhat longer than a day. The effect is marked with a 5 per cent solution. It is very marked with a 10 per cent solution. A 20 per cent solution may be used, although this concentration seems to give an unpleasant effect, ranging from slight discomfort to a subjective feeling of headache and slight nausea, which, however, disappears from one-half to one hour.

COMMENT

In our experience furfuryl trimethyl ammonium iodide has been shown to be a potent parasympathetic drug and especially so in bringing about a reduction of the intraocular tension. It seems to us, therefore, that this drug is worth a trial in the treatment of glaucoma, since it seems likely that the effect in cases of ocular pathologic involvement will be much more marked. Such preliminary work as we have done indicates that it is probably more effective than any of the drugs at present used and that it is entirely safe.

Smith, Kline and French Laboratories supplied us with furfuryl trimethyl ammonium iodide (furmethide).

EFFECT OF IONTOPHORESIS ON THE EYE

WITH SPECIAL REFERENCE TO INTRAOCULAR TENSION

WILLIAM THAU, M.D.

AND

ABRAHAM MYERSON, M.D.

BOSTON

Iontophoresis as an important method of producing physiologic phenomena and of introducing chemical substances into the body was first utilized by Leduc.[1] This investigator pointed out that bodily phenomena were in essence electrical and that iontophoresis was a means of introducing ions into the organism and modifying the prevailing ionic relationship. This paper is the classic start of a long series of investigations. No attempt will be made in this paper to review the literature.

In respect to ophthalmology, Wirtz[2] developed a technic by which the galvanic current was used to introduce chemical substances into the eye and thus to treat various diseases of the eye. He made no study of the influence of iontophoresis on intraocular pressure, nor did he use sodium chloride, which is the basis for the work here reported.

Cantonnet[3] used drugs by means of the galvanic current in the form of iontophoresis to reduce the intraocular tension and stated definitely that various chemicals induced in this manner lower intraocular tension. He also mentioned favorable results obtained in simple glaucoma by this means. So far as we know, he is the only investigator who particularly studied the problem of intraocular tension and its relationship to iontophoresis, although only with chemicals.

There is a long series of papers dealing with iontophoresis, mainly in the foreign literature.[4] As stated previously, the work has been

1. Leduc, S.: Introduction des substances médicamenteuses dans la profondeur des tissus par le courant électrique, Ann. d'électrobiol. 3:545-560, 1900.

2. Wirtz, R.: Die Ionentherapie in der Augenheilkunde, Klin. Monatsbl. f. Augenh. 46:543-579, 1908.

3. Cantonnet, A.: L'ionisation de l'oeil. Technique et résultats, Rev. gén. de clin. et de thérap. 41:113-116, 1927.

4. Brünner-Ornstein, M.: Ueber neuere Methoden der Iontophorese, Wien. klin. Wchnschr. 48:822-824, 1935. de Grósz, E.: L'ionisation au glaucosan, Arch. d'opht. 53:25-31, 1936. de Raadt, O. L. E.: Untersuchungen ueber hydropigene

mainly in relationship to diseases of the eye and has not been specifically directed to various ocular phenomena, including intraocular tension.

PRESENT STUDY

This research is part of a series of papers dealing with the relationship of autonomic drugs to the physiology of the eye and especially the intraocular tension. In previous papers [5] we pointed out that intraocular tension is distinctly lowered by the parasympathetic drugs, prostigmine and mecholyl, and raised by benzedrine sulfate, epinephrine hydrochloride, atropine and other sympathomimetic drugs. The present research grew out of the observation that the effects of iontophoresis on intraocular tension were independent of the chemicals we used. When distilled water was used, the intraocular tension was lowered. Finally, because of the need to maintain physiologic conditions of the eye, physiologic solution of sodium chloride was selected as the chemical compound introduced by the galvanic electric current.

TECHNIC

A specially shaped, spoonlike, copper electrode, covered heavily with absorbent cotton and kept thoroughly moistened by physiologic solution of sodium chloride, was placed lightly on the lower fornix and kept in contact with the lower half of the ocular globe. Care was taken not to touch the cornea. This site was selected because the electric current can be more easily applied without endangering the cornea, and this structure can be closely watched during the entire period of iontophoresis. The cornea is sensitive to the electric current, and all investigators, including ourselves, have found that damage to the cornea can easily take place. In one of our experiments a clouding of the cornea resulted, which was, however, successfully and easily treated, with no residuals. If care is taken and the cornea watched at frequent intervals (one to two minutes), no injury to the cornea will occur.

The results are obtained by the introduction of sodium chloride either by the positive galvanic current or by the negative current. It is probable that the negative galvanic electrode is more effective, but the effects of either positive or negative galvanic electricity are notable. The dose is from 5 to 10 milliamperes for a period

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Ionenwirkungen auf lebende Gewebe mittels Durchströmung im Tierversuch, München. med. Wchnschr. **80**:778-779, 1933. Erlanger, G.: Elektrische Einverleibung von Pharmaka (Iontophorese) ins Auge, Jahresk. f. ärztl. Fortbild. (no. 11) **23**:22-24, 1932. Krückmann, E.: Ueber Verwendbarkeit der Kataphorese zur lokalen Behandlung leutischer Augenerkrankungen, Ztschr. f. Augenh. **11**:13-32, 1904. Stallard, H. B.: Katholysis in Treatment of Retinal Detachments: Preliminary Note, Brit. J. Ophth. **21**:35-44, 1937. Strebel, J.: Technische Fortschritte in der Iontophoresebehandlung, Klin. Monatsbl. f. Augenh. **86**:662-665, 1931.

5. Myerson, A., and Thau, W.: Human Autonomic Pharmacology: IX. The Effect of Cholinergic and Adrenergic Drugs on the Eye, Arch. Ophth. **18**:78-90 (July) 1937. Myerson, A.: Human Autonomic Pharmacology: XII. Theories and Results of Autonomic Drug Administration, J. A. M. A. **110**:101-103 (Jan. 8) 1938.

ranging from eight to fifteen minutes. The effect locally is usually an injection of the capillaries of the conjunctivas. This effect wears off within a few days and is not painful or disturbing to the patient. In addition to the injection, there sometimes appears a slight edema of the fornix, which lasts a short time (about twenty-four hours) and is without any untoward effect on the patient.

RESULTS

There is a general parasympathetic effect, namely, slight narrowing of the palpebral fissure, a lessening of the size of the pupil, some anterior projection of the lens and a definite and durable dropping of the intra-ocular tension. These results were obtained consistently and repeatedly on 4 patients with tractable dementia praecox and are presented in the

Typical Effects of Iontophoresis on the Eye

			Number of Milli-am-peres	Dura-tion, Min.	Effect on					
Case	Eye Used	Cur-rent			Palpebral Fissure	Conjunc-tivas	Anterior Chamber	Pupils, Mm.	Intra-ocular Tension (Schiötz)	Length of Effect, Days*
1	Right	+	5	14	Narrower than left	Hyper-emia; slight lacrima-tion	Deeper than left	R. 2 L. 5	R. 22 L. 32	5
2	Right	+	7	14	As in case 1	As in case 1	As in case 1	R. 3 L. 5	A. 20 L. 28	6
3	Left	—	7	15	Narrower than right	As in case 1 with slight edema	Deeper than right	R. 4 L. 2	R. 20 L. 16	5
4	Left	—	8	15	As in case 3	As in case 3	As in case 3	R. 4 L. 2	R. 23 L. 16	9

* The effect daily diminishes until the original tension finally returns.

accompanying table. With the positive electrode, the effects last from five days to a week, and with the negative electrode from six to nine days.

It will be seen that the lowered intraocular tension thus obtained is much more durable than that obtained by drugs, since with any of those now in use the effects last only a few hours. Our repeated experiments on the same persons have shown no dangers to this method, if care is constant and the electrode is kept from contact with the cornea. Necessarily, the electrode must be kept constantly moistened with the salt solution.

COMMENT

We are here broaching no theories as to the nature of the phenomena by which these results are obtained. Obviously, with the positive electrode the ions discharged into the eye, if salt solution is used, are the

sodium ions. However, if the negative pole is used the chloride ions enter the local structure of the eye. Thus, negative and positive charged ions seem to produce the same general results. The effect may possibly be a stimulation of the ciliary muscle by the parasympathetic nerve and may be linked up with the increased blood flow,[6] as evidenced by the dilatation of the capillaries, or may have reference to some more obscure and less ascertainable chemical changes within the reacting cells themselves. Whatever the mechanism, the effect seems to us to be noteworthy and worthy of clinical extension into the treatment of glaucoma. It is likely that iontophoresis will produce a more marked reduction in the eye with this pathologic condition than in the normal eye.

6. Evans, P. J.: Underlying Causes of Glaucoma Including Notes on Lines of Enquiry Which Have Been Pursued, with Suggestions as to Future Research in Clinic and Laboratory, Brit. J. Ophth. 23:745-783, 1939.

CHOROIDAL "PERITHELIOMA" SIMULATING RETROBULBAR NEURITIS

REPORT OF A CASE

BENJAMIN FRIEDMAN, M.D.

NEW YORK

The facts relating to the case reported here are unusual in several respects. First, the changes in the visual field and the nasal findings led to an erroneous diagnosis of retrobulbar neuritis due to sinus disease. Second, evidence of tumor was not noticed until eight months after the initial complaint. Third, at no time did the ophthalmoscopic examination of the macular area reveal any abnormality to account for the defect of the central field. Fourth, the microscopic appearance of the tumor was sufficiently unique to warrant a report on its own account.

REPORT OF CASE

Mrs. B. E., aged 64, presented herself on March 28, 1938, with the complaint that for a week she had noticed a shadow in front of the right eye. The obscuration was constant in its location and did not have the characteristics of an opacity of the vitreous. Moreover, the visual impairment appeared to her to be increasing. The only other significant part of her history was the statement that she did not suffer from colds more frequently than the average person and that she did not have a cold or nasal discharge at the time. The corrected vision was 20/50 + in the right eye with a + 0.75 sph. $\subset$ + 0.50 cyl., ax. 180 and 20/25 in the left eye with the same correction.

Examination of the right eye disclosed early peripheral opacities of the lens. There was advanced retinal arteriosclerosis but no retinal lesion either in the macula or elsewhere. The disk was normal in appearance. A similar picture was seen in the left eye.

Plotting of the central visual field of the right eye disclosed a spindle-shaped scotoma starting at the fixation point and extending downward and temporally as far as the 25 degree circle. The lower nasal border of the blindspot was connected to the middle of the defect. The blindspot was not otherwise enlarged, and the peripheral visual field was unbroken.

Physical examination, including a nasal examination by the family physician, revealed no pertinent data. The usual laboratory tests gave negative results. Since no specific treatment seemed obvious, it was decided to treat the patient empirically with acetylcholine, and a course of twelve injections on successive days was administered. Not the least benefit resulted.

A special investigation of the nose and throat was undertaken on May 13 by a capable and reliable rhinologist, who found the following conditions: Polyps in the right middle meatus, a deviated septum, dark antrums on transillumination

and embedded tonsils. Irrigation of the right frontal sinus revealed pus. A roentgenogram of the sinuses showed a cloudy right frontal sinus. A diagnosis of right ethmoiditis and frontal sinusitis was made.

In view of the positive rhinologic evidence, I felt justified in the diagnosis of retrobulbar neuritis due to sinusitis and advised operation.

On May 20 a right sphenoethmoid antrotomy was done, local anesthetization being employed. The ethmoid cells were found to contain polypoid material.

The patient was given the usual postoperative treatment of irrigation and tamponage of the sinuses. Irrigation of the right frontal sinus, however, never produced a perfectly clear return.
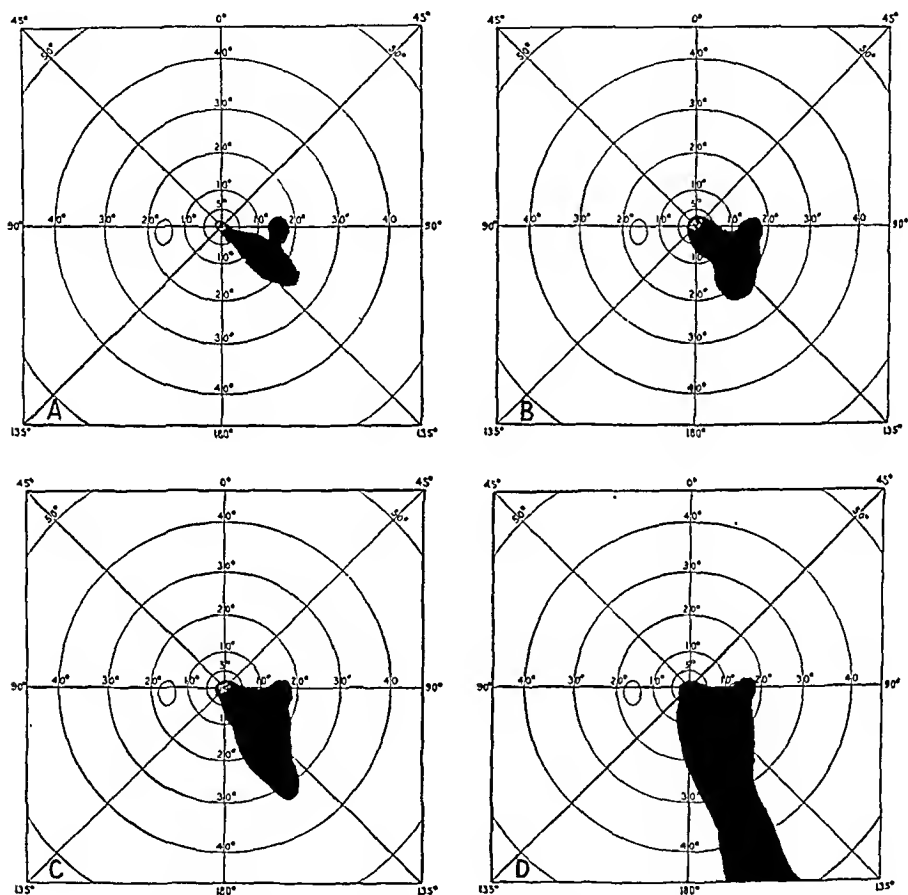
Fig. 1.—Tangent screen scotometry. *A*, the field on March 28; *B*, the field on May 5; *C*, the field on June 3, and *D*, the field on December 5. The scotomas in *A*, *B* and *C* antedate the ophthalmoscopic visibility of the tumor. *D* shows the changes in the central field after the growth became visible.

The visual acuity remained at 20/50 —. During the entire summer of 1938 the patient faithfully subjected herself to nasal cleansings and repeated injections of acetylcholine and nitroscleran (sodium nitrite to which another inorganic salt had been added), she ingested large quantities of vitamins and submitted to numerous ocular examinations. Still her vision did not improve. On the contrary, although her record with the Snellen chart did not indicate retrogression, she insisted that the shadow was growing larger. Her complaint was

substantiated by a progressive enlargement of the scotoma. My last note at this stage is dated September 10, about five and one-half months after I first saw her. The fundus was still normal. The patient justifiably grew discouraged and did not return until December 5, about eight months after the onset of her disturbed vision.

An alteration in the fundus picture had occurred in the interim. A circular elevation of the retina was visible above and temporal to the optic nerve at about 3 disk diameters from the nerve head. Its area was about the size of the disk. The elevation was inconspicuous, perhaps 1 D. in height at its summit, and several
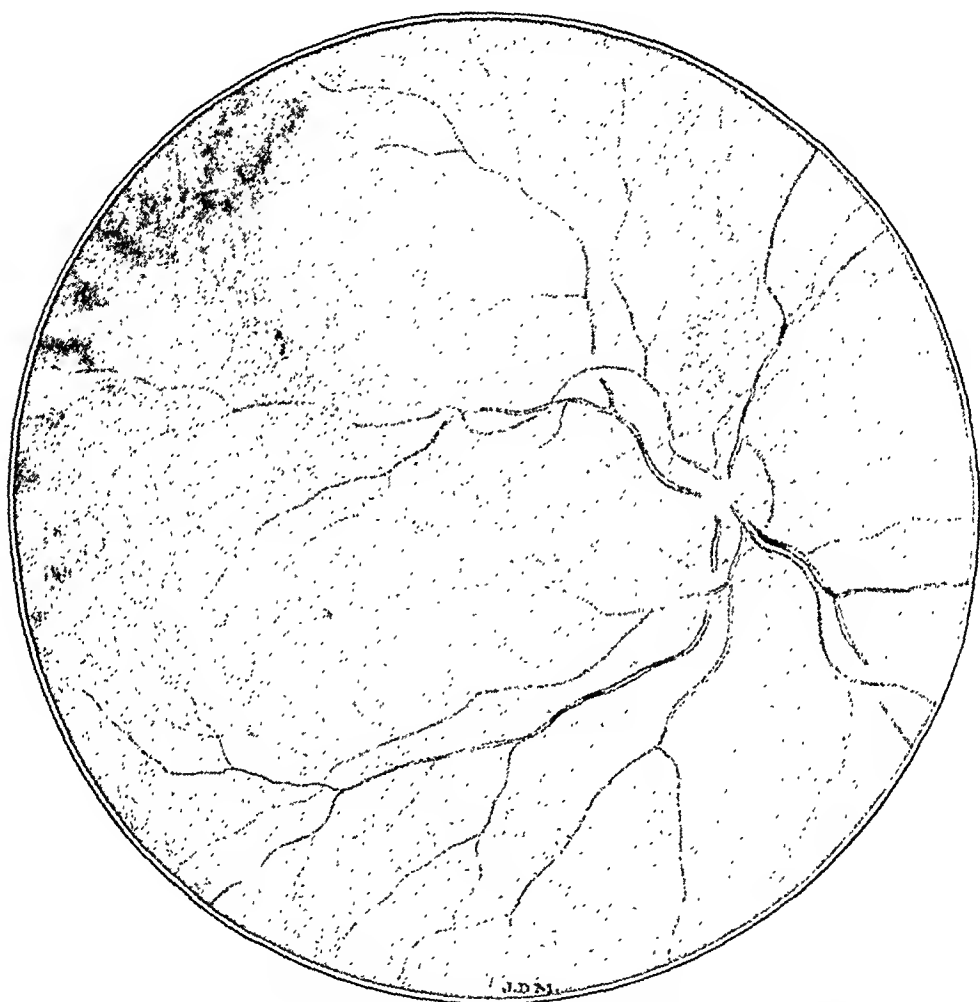
Fig. 2.—Appearance of the fundus just prior to enucleation.

grayish yellow lesions at its upper border hinted at a massive choroiditis rather than a tumor. The main area of the elevation was not discolored. Slit lamp study of the vitreous and retrolental space revealed no pigmented bodies, and the cornea was free from deposits. The macula was normal in appearance, and the retina between the nerve and the mass appeared also to be normal. The diagnosis of tumor was considered but held in abeyance because of the peculiar changes in the visual field which antedated the lesion in the fundus and because the retinal mass in some respects affected the appearance of choroiditis.

Two months later (Feb. 7, 1939) the elevation of the mass had increased to 5 D., and its circumference had doubled. The vision fell to 20/70. The macular area was still normal in appearance. The scotoma was definitely enlarged. The

tension was normal and equal in both eyes and remained so.   Long before this
the true nature of the fundus picture had become only too obvious, but the patient
was reluctant to have the eye removed.

On March 20, almost exactly one year after the beginning of this chronicle,
the vision was reduced to 20/200, and the retina between the tumor and the disk
appeared elevated.   It is important to reemphasize that the region of the macula
was normal, even when viewed with the Gullstrand binocular ophthalmoscope, and

Fig. 3.—Detachment of the retina at the macula.

the retina between the tumor and the macula gave no evidence of detachment,
infiltration or edema.   The macula was separated from the mass by about 2 disk
diameters of retina.   The tumor had increased in height to an elevation of
about 8 D.   The optic nerve was normal, and there was no suggestion of atrophy.
The patient had in the meantime consulted two other oculists and at this point
consented to enucleation.

Histologic Report (Dr. L. von Sallmann).—The eyeball was fixed in Zenker's
solution and embedded in pyroxylin celloidin.   Complete serial sections were cut
horizontally.

The anterior part was normal except for cystlike formations of the ciliary processes.

The choroid was normal except for the area of the tumor, which lay in the upper temporal quadrant and measured about 4.5 mm. horizontally and was 2.5 to 3 mm. thick. It almost reached the ora serrata in the upper periphery and lay with its lower margin about 3 mm. above the horizontal meridian. The growth consisted mostly of tubes and solid columns of large elongated cells with ample
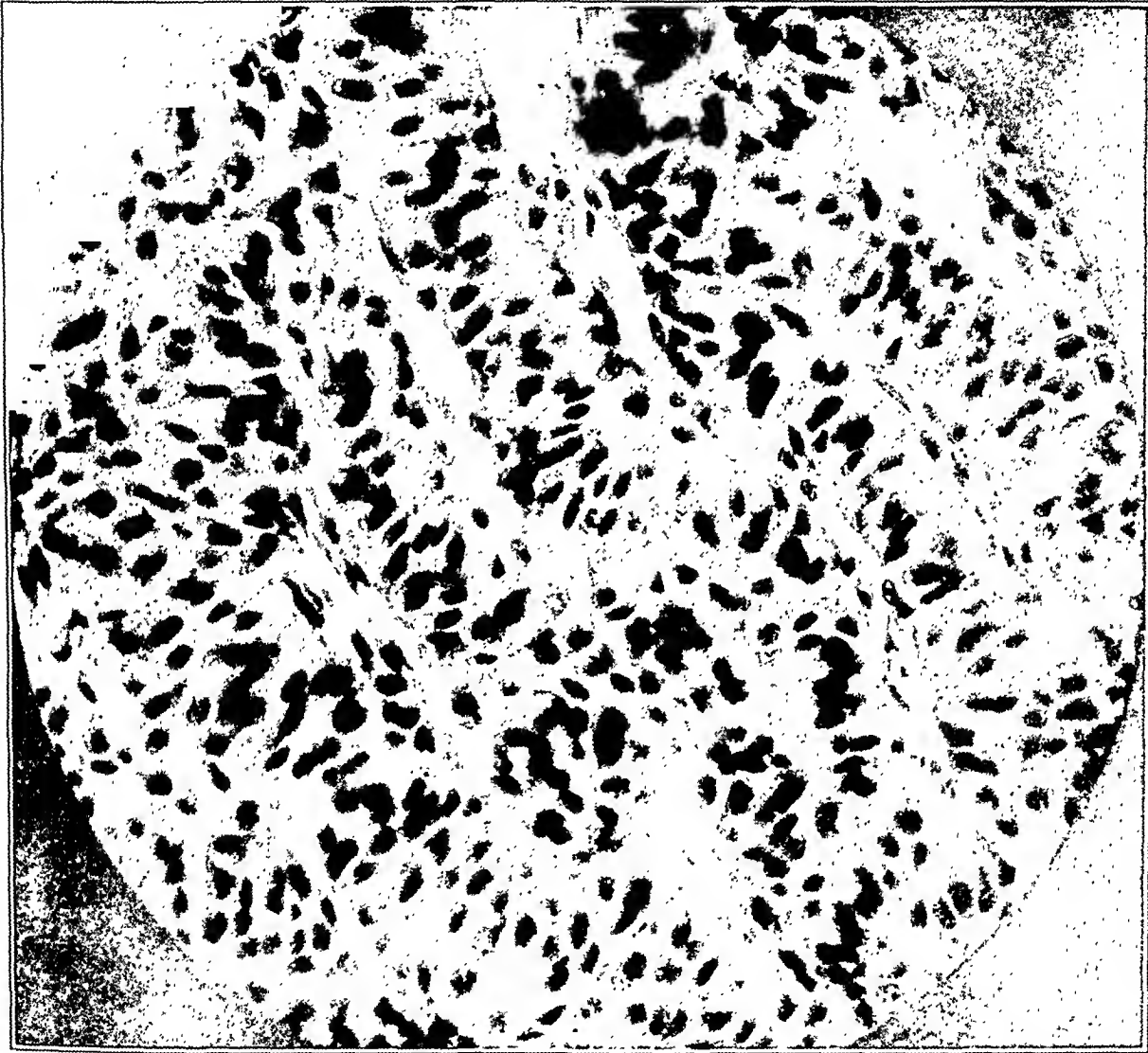
Fig. 4.—The cellular structure of the tumor under high magnification.

protoplasm, and oval nucleus and a distinct nucleolus. The nuclei showed a certain degree of polarity. The cells were mostly arranged in palisades around fine lumens, many of which were partly filled with blood. The tubes seemed to be twisted around each other, so that they appeared as pseudorosettes on cross section. In the central area the palisade arrangement diffused into irregular small groups of polygonal and round cells. In the marginal portion of the tumor flat cells with scanty bluish-stained protoplasm and elongated nuclei were arranged in concentric layers. This type of cell intruded into the main mass of the tumor. In the peripheral richly vascularized part of the tumor a connective tissue frame-

work was found which extended in the form of fine strands into the central portion, mostly in connection with thin-walled vessels. In the outer layers of the tumor many pigment cells were interspersed, but few pigmented cells lay in the main bulk of the growth. The stain for argyrophil fibers showed a dense reticulum only in the peripheral portion and no fibers in the central part of the tumor.

In the sclera tumor cells in groups were found in lymph spaces around blood vessels. Between such spaces the sclera seemed normal, and the outer third was apparently not at all involved.

The retina showed moderate peripheral cystic degeneration. Besides an artificial detachment caused by the fixative, a flat serous detachment lay in front of the choroidal tumor and in its neighborhood. The detachment reached the upper circumference of the optic nerve and extended into the macular area. Here the detachment was a higher one, and the subretinal fluid assumed a cone-shaped formation. From the macula the detachment extended to the lower half of the retina in the form of a small stripe, which gradually became flatter and narrower. In addition to this central detachment, the retina was detached in the temporal periphery between the ora serrata and the equator and to a much lesser extent in the lower nasal quadrant. Cones and rods were more or less destroyed in the detached area. The outer granular layers were here somewhat rarefied, and the pigment epithelium showed the usual signs of degeneration and proliferation. The changes were especially prominent in front of the tumor.

The optic nerve was somewhat edematous but did not show inflammatory or degenerative changes (Weigert's medullary sheath stain).

The tumor corresponds most closely to the classic description of the perithelioma, and it may be called so if this name means only a morphologic and not a histogenic entity. It belongs to the group of epithelioid melanomas which are classified by French authors as neuroepitheliomas.

Changes in the visual field corresponding to the location of the tumor are to be expected in a choroidal growth, but it is unusual for such defects to be manifest without the ophthalmoscopic evidence of the tumor. It is much more unusual for such defects to begin as, or even to include, a central scotoma, where the mass is remotely extramacular in origin. There are cases on record of eccentrically located growths in which a central scotoma existed, but this was accounted for by secondary pigmented lesions in the macula. In the present case the macula appeared healthy on ophthalmoscopic examination at all times. The microscopic evidence made it clear that the changes in the central field were due to a shallow detachment of the retina in the region of the macula by the fluids exuding beyond the margins of the tumor. The effect on the vision was manifest eight months before the growth revealed itself; the macular detachment escaped clinical recognition altogether. The coincidental positive rhinologic findings in particular were misleading, and they were responsible for an unnecessary operation on the sinuses. The fact that despite nasal operation the vision steadily deteriorated and the scotoma expanded proves that the sinusitis was latent in nature and unconnected with the visual disturbance. Microscopic examination of the optic nerve bore this out. Once the tumor made itself evident

ophthalmoscopically, its enlargement was extremely rapid, having increased in elevation from 1 to 8 D. in less than four months. The circumference of the tumor at its base more than doubled.

It was interesting to note the unusual line of the level of the sub-retinal fluid. The fluid appeared prismatic in cross section, a behavior certainly at variance with the expected even level. The apex of the prism lay under the macula. It was interesting also that the neuroepithelium over the summit of the subretinal fluid appeared considerably less damaged than in the less elevated region nasal to it. Unusual also was the great distance to which the fluid early gravitated in order to reach the macula, at the time the initial symptoms appeared, and it is hard to explain why it was held in a narrow confine so long without causing more widespread detachment.

The patient was in good health at the time this report was written. It was then ten months since the eye had been removed and twenty-two months since the first warnings of the tumor. Periodic physical examinations, augmented by roentgenograms of the chest and bones, have disclosed no evidence of metastasis or of a possible primary growth elsewhere.

ENCANTHIS TRACHOMATOSA

EMIL OLÁH, M.D.

Chief Ophthalmologist, State Hospital

GYULA, HUNGARY

Regardless of how long the duration of the disease, sooner or later trachoma heals in response to suitable treatment. However, there occasionally are patients who have apparently been cured of trachoma whose eyes periodically become teary and redden in response to the slightest touch. Eversion of the lid for examination of such eyes is sufficient to excite them, but inspection by this method frequently does not yield any information as to the cause of the disturbance. The conjunctival sac is thinned and finely scarred, as it usually is after a trachomatous lesion heals. If the nasolacrimal duct is unobstructed, there is not a shadow of doubt that the trachoma has entrenched itself in one of its usual hiding places, probably in the tarsus. The lacus lacrimalis and its structures are not given the consideration they deserve as a hiding place for trachoma. Examination of every part of this area should be made when a patient who is apparently cured of trachoma has complaints referable to the eye.

Trachoma of the lacus lacrimalis and its structures is frequently resistant to treatment and is independent of trachoma of the conjunctival sac. By this is meant that trachoma of the conjunctival sac is cured, but in the angulus medialis it not only resists treatment but develops farther. In connection with this, two questions arise. 1. Does trachoma of the angulus medialis really behave independently of trachoma of the rest of the conjunctival sac? 2. Regardless of whether this condition is real or apparent, how does it develop?

On digital separation of the lids, the conjunctiva in the medial angle is frequently apparently undamaged. However, if the lids are separated at their medial third with a rounded double hook, thereby revealing the medial angle, and the examined subject is made to look sideways, trachomatous changes may be found in the lacus lacrimalis even if the rest of the conjunctiva has been considered clinically cured after years of treatment. The fact that the conjunctival sac may apparently be cured while the conjunctiva of the medial angle remains trachomatous has been ascertained on innumerable occasions. It is an everyday occurrence in cases in which trachoma has been treated for a long time to find serious changes in the conjunctiva of the medial angle and minimal changes

in the rest of the conjunctiva. This observation is supported by the publication of Scardanapane, who found that trachoma continues to develop in the plica even if scarification has commenced in the rest of the conjunctiva. Furthermore, Tóth[1] observed cases in which the trachoma limited itself to the plica, canaliculi and the conjunctiva of the medial angle. The question may also arise as to what is hidden in the tarsus behind the cured conjunctiva. From the studies of Kacsó[2] on specimens of excised tarsus it was learned that trachomatous infiltrations were found in the tarsus and principally between the conjunctiva and the tarsus. In practice, the question is what should be done in such a case. Naturally if the conjunctival sac is apparently healed, the position of the lids is normal or there is only a small degree of ptosis; however, if trachomatous changes are found on the conjunctiva of the medial angle, all efforts should be directed toward the cure of the trachomatous changes in the tarsus as quickly as possible, irrespective of the other trachomatous changes. If one seeks the cause for serious trachomatous change around the lacus lacrimalis and its structures after the rest of the conjunctival sac has healed, or for trachomatous changes in the lacus lacrimalis which are serious in relation to those in the rest of the conjunctival sac, the only answer that can be found is that the lacus lacrimalis is more difficult of access to the present surgical technics than the rest of the conjunctival sac. Studies have been made of the accessibility of the lacus lacrimalis to medical treatment as compared with the ease of medication of the fornix conjunctivae. These studies were first made on healthy persons and later on patients with trachoma which had extended to the medial angle and its structures. A piece of white filter paper 2 mm. square was placed in the depth of the fornix and the lacus. The technic employed is similar to that employed in the treatment with silver nitrate. Eosin was dropped on the conjunctiva of the everted upper eyelid. When the conjunctiva was healthy there was no difference in the staining of the filter paper placed in the fornix and that placed in the lacus. In the case of patients with trachoma whose semilunar plica was swollen, it was frequently found that the filter paper placed in the depth of the fornix was dyed, whereas that placed in the lacus was not stained or was slightly stained. It may also be added that the lateral angle is easily accessible to surgical and medical intervention; naturally I have as yet not found a case in which the trachoma was localized in the external angle after the rest of the conjunctiva was healed.

1. Tóth, Z.: Ueber die Tränenabflusswege bei Trachoma, Klin. Monatsbl. f. Augenh. **91**:685, 1933.

2. Kacsó: Untersuchungen an trachomatösen Tarsusknorpeln, Klin. Monatsbl. f. Augenh. **69**:140, 1922.

According to Lenhossék, the lacus lacrimalis is limited by a low smooth fold of skin, and its base is covered by conjunctiva. To this description should be added the fact that medial to the punctum lacrimalis the fold of skin does not contain any of the tarsus. However, this region cannot be simply designated as a fold of skin, as it is lined with conjunctiva which is a continuation of the tarsal conjunctiva. If the fold of skin bounding the lacus lacrimalis is pulled apart, it becomes evident that the conjunctiva lining the lacus is deeper at its commencement (3 mm.) and gradually loses its depth in the medial direction. The conjunctiva of the fold of skin continues in the epithelium of the caruncula lacrimalis, and its reflection is linear. Medially, the epithelium of the caruncula continues into the epithelium of the fold of skin without the presence of intervening conjunctiva or a dividing groove.

Trachomatous change in the lacus lacrimalis and its structures may vary as compared with those in the other parts of the conjunctival sac. This region includes the plica, the conjunctiva lining the base of the lacus and the fold of skin bordering the lacus and the caruncula. I have observed only infiltration on the plica but no follicles. There was no hypertrophy on the plica, not even when the conjunctival sac had been covered for years with an excessive papillary hypertrophy, which could not be influenced by treatment. The conjunctiva of the lacus is slightly inflamed and swollen, even in the cases of mild involvement. I have found hypertrophy of the conjunctiva of the lacus on microscopic study but not macroscopically. Follicles of semilunar shape were found close together in the root of the caruncula. Sometimes, especially in cases in which treatment had been given, only occasional follicles were found. There was no hypertrophy of the caruncula. According to my experience, trachomatous inflammation involves the caruncula. I have observed cases in which this occurred, and since they are unusual reports of them are deserving of publication.

REPORT OF CASES

CASE 1.—A man aged 20 had been treated surgically several times years ago for trachoma. He had considered himself cured for years and had had no complaints until a few months before his entry to the hospital, at which time a tumor appeared in the medial angle of the eye. It grew slowly, and weeks before his admission it extended in front of the lid and into the palpebral fissure, preventing complete closure of the lids.

The conjunctivas of both eyes were smooth, thinned and cicatrized. In the right eye a structure similar to a horn of skin projected from the medial angle. On first glance it appeared to be different from a cornu cutaneum despite its many points of similarity. The formation was 11 mm. high and wider at the base; farther up it was uniformly 3 mm. wide, with a rounded end. It originated from the conjunctiva of the medial angle, embracing the caruncula but having nothing to do with the fold delimiting the lacus. Between it and this fold of skin was a

groove, which at its medial end passed into the skin without any limiting border. It deepened by degrees toward the punctum lacrimalis. With the exception of its foundation, the growth was parchment dry and brownish red. No typical stratification or circular or longitudinal grooves could be seen. The structure was soft to the touch. It therefore could not have been a cornu cutaneum, because it differed from that in every respect except its similarity in form. Since it could not be a cutaneous horn, I thought that it might be a follicle, as it was soft, and that owing to the swelling of the caruncula it might have gotten in the palpebral fissure, assuming its present form as a result of the movement of the lids. Therefore, I decided to express it. Counting on the possibility that on expression it might not behave like a trachomatous follicle, and in order to preserve the formation for later histologic study, I started expression only at the tip of the structure, previously injecting an anesthetic into the conjunctiva of the medial angle. After expression of the tip of the formation, the structure containing the expressed part collapsed like a balloon that had been deflated. After this the rest of the formation was expressed, with similar results, but I could not reach the base of
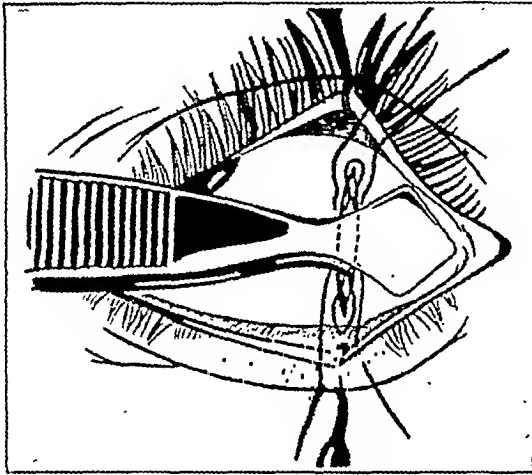
Fig. 1.—Drawing showing the technic of expressing the conjunctiva of the base of the lacus and the caruncula lacrimalis and the type of expressor used.

the structure with the expressor. I decided to introduce one edge of the instrument under the conjunctiva and the other above it so that I could express the entire conjunctiva of the medial angle and its structures. After the lids had been drawn apart with two hooks, a vertical incision, 1 cm. long, was made in the conjunctiva with a scissors 1 mm. medial to the plica. I immediately introduced two sutures into the incision. Holding the sutures taut, I introduced a small straight scissors between the two sutures and prepared a path for the expressor, a triangular-shaped instrument of small dimension, by cutting with the scissors toward the medial angle (fig. 1). I then expressed the conjunctiva of the base of the lacus and of the caruncula. After expression of this structure, the conjunctiva at its site was found to be wrinkled, but a few days after the removal of the sutures it had the appearance of normal conjunctiva. On inspection a year later, the medial angle was found to be normal. The caruncula was somewhat smaller than that on the other side. A diagnosis of encanthis trachomatosa was made.

CASE 2.—A 30 year old woman was sent to the hospital for the removal of a tumor of the eyeball. She had been treated for trachoma for years; of late years the condition had been thought to be completely cured, because she had no

complaint. A few months before her admission to the hospital a slowly growing tumor appeared in the medial angle of the right eye. The eye could be closed. The conjunctiva of the upper fornix was cicatrized, and an occasional follicle was present. There was a papilloma-like tumor filling the medial angle and the lacus lacrimalis, including the caruncula. The tumor was soft to the touch, not hard like a papilloma. It appeared to be a mass of trachomatous follicles, which assumed its tumorous shape due to the anatomic relations around its place of origin. I performed a transconjunctival expression in the manner described in case 1, and a loosely grooved conjunctiva remained in the place of the tumor. The conjunctiva assumed its normal appearance after a few weeks. The caruncula was of normal size.

With reference to the technic of transconjunctival expression, I might add that the incision made in the conjunctiva is not always medial to the plica. If the plica itself is infiltrated, the incision is made between the plica and the limbus. Of course, if there are any trachomatous follicles on the bulbar conjunctiva that are not accessible and are not near the medial angle, these, too, are expressed by introducing one of the edges of the expressor under the conjunctiva.

CLINICAL EVIDENCE

In support of the fact that the caruncula lacrimalis plays a part in trachomatous inflammation, a whole series of clinical observations can be reported. In the 2 cases reported here no histologic studies were made, but the healing consequent to expression tends to prove that the formation observed on the caruncula was nothing more than a mass of trachomatous follicles peculiarly shaped by the nature of their surrounding. If the carunculae of a great number of patients with trachoma are examined clinically data will be obtained that permit of no conclusion other than that the caruncula lacrimalis has a part in the trachomatous inflammation. Clinical examination leaves much to be desired as regards the exactness of the details of the process, but even so the extreme stages may be well observed. After the conjunctiva has become infiltrated and thickened, the caruncula follows suit and often even becomes swollen. In contrast to this, examination of a patient with trachoma of years' standing which is largely cicatrized, with resulting atrophy or xerosis of the conjunctiva, may show that the caruncula too has become atrophied. It is certain that the course of the trachoma of the caruncula does not parallel that of the trachoma of the conjunctival sac; however, I have observed in more than one case that the trachomatous caruncula is so atrophied that it is not elevated above the conjunctiva of the lacus, so that one can only suspect its location. If the fold limiting the lacus is pulled away with a rounded hook, the site of the caruncula is a grayish yellow spot in the conjunctiva of the lacus.

My histologic observations presented later in this paper indicate that the caruncula has a part in the trachomatous inflammation of the

conjunctival sac. Textbooks neglect this question. However, available published data do not exclude the possibility.

Hiwatari[3] reported a case of cicatricial trachoma in which a tumor consisting of lymph nodes appeared in the caruncula, which he considered to be of trachomatous origin.

Van Scheevenstein reported the occurrence of a hyaline tumor on the caruncula, which he considered trachomatous.

Thus it is seen that other authors assume, in given cases, the existence of trachomatous inflammation of the caruncula. The condition in the first of my 2 cases reported here could not have been anything but encanthis trachomatosa; this assumption was supported by the healing consequent to expression. Observations of the caruncula at some time after each stage of trachomatous inflammation—inflammation, infiltration, cicatrization and atrophy—also support the assumption that the caruncula takes part in the trachomatous inflammation. My observations are supported by those of Scardanapane and Van Scheevenstein. To decide the question, histologic studies were made, since I felt that clinical observations were inadequate.[4]

HISTOLOGIC EVIDENCE

The description of several preparations are presented. I studied a total of thirty, but since I repeatedly noted the same thing in a number of the sections, I feel that it is unnecessary to describe any more. I could not examine a caruncula from a patient with fresh trachoma or with trachoma of few weeks' or months' standing. However, I hope to have such preparations eventually. These preparations were obtained as follows: The caruncula and a small part of the conjunctiva of the lacus were outlined with a knife and excised with a scissors. The sections were made of the entire caruncula in a horizontal plane. In this way the conjunctiva of the lacus was also included.

CASE 1.—L. A., a married woman, suffers from long-standing trachoma and periodic pannus of both eyes. She is at present a psychiatric patient and so is periodically untreatable. Examination at the time this study was made revealed scarred conjunctiva with occasional follicles in the upper fornix. The caruncula was medium in size. Between the caruncula and the fold delimiting the lacus lacrimalis there was a symblepharon caused by scar tissue.

A specimen was excised as described and sections made (Van Gieson's stain). There was much inflammatory infiltration under the epithelium, which caused thinning in spots (fig. 2). A follicle of lymphocytes was observed under the epithelium; this had no capsule and no typical structural characteristics. Much

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3. Hiwatari, K.: Trachomatous Changes of the Caruncule, Am. J. Ophth. 2:243, 1919.

4. Dr. Karoliny, chief pathologist at the State Hospital, prepared, photographed and studied the microscopic sections.

deep scar tissue could be seen. Occasionally processes extended from the scar tissue toward the epithelium. Under the epithelium the processes appeared with inflammatory infiltration. In the scar tissue itself no glandular structure could be observed. However, on the margin of the scar tissue hair follicles and sebaceous glands cut in various planes could be seen. In addition to the scar tissue, the excretory ducts of sweat glands could be observed with columnar cells within, flatter reserve cells behind the columnar cells and a basilar membrane which stained red.
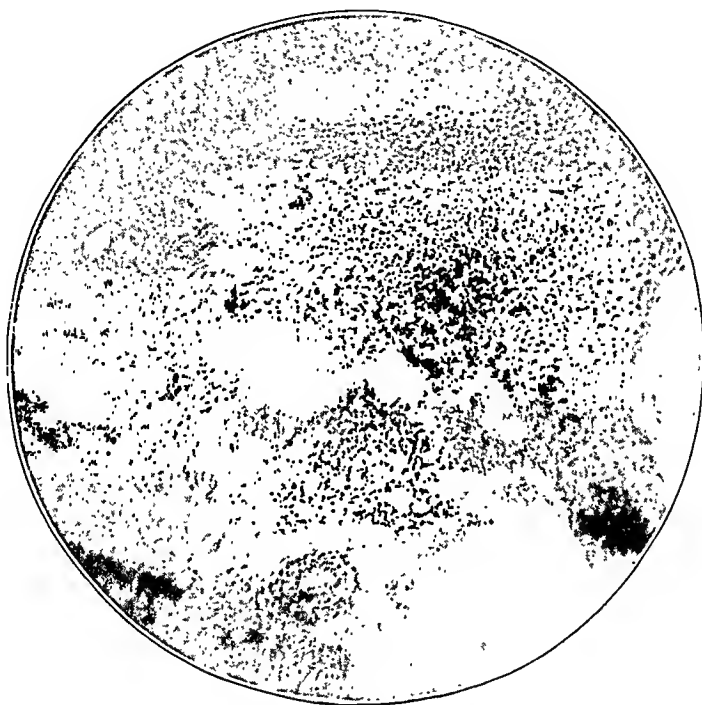
Fig. 2.—Inflammatory infiltration under the epithelium, with thinning of the epithelium in spots.

CASE 2.—F. V. had trachoma of many years' standing; it was slightly follicular in type and principally papillary. The condition had responded only slightly to medical, mechanical and operative treatment.

Scar tissue could be well seen in the caruncula; this continued into the scar tissue of the conjunctiva of the base of the lacus beyond the caruncula (fig. 3). In the root of the caruncula there were several papillae at a level lower than the caruncula. The scar tissue extended to the base of the papilla but did not extend to the papilla itself.

Material taken from this patient showed immediately under the epithelium a follicle of lymphocytes surrounded by a capsule of scar tissue (fig. 4). The trachomatous follicle stretched toward the center of the caruncula. Immediately next to it, but separated by scar tissue, was another trachomatous follicle. It consisted mainly of lymphocytes with granulation tissue cells, which took a lighter stain, and was elongated at both ends (fig. 5). This follicle, too, was surrounded by scar tissue. Opposite to the follicle on the other side of the scar tissue there were sebaceous glands cut in various planes.
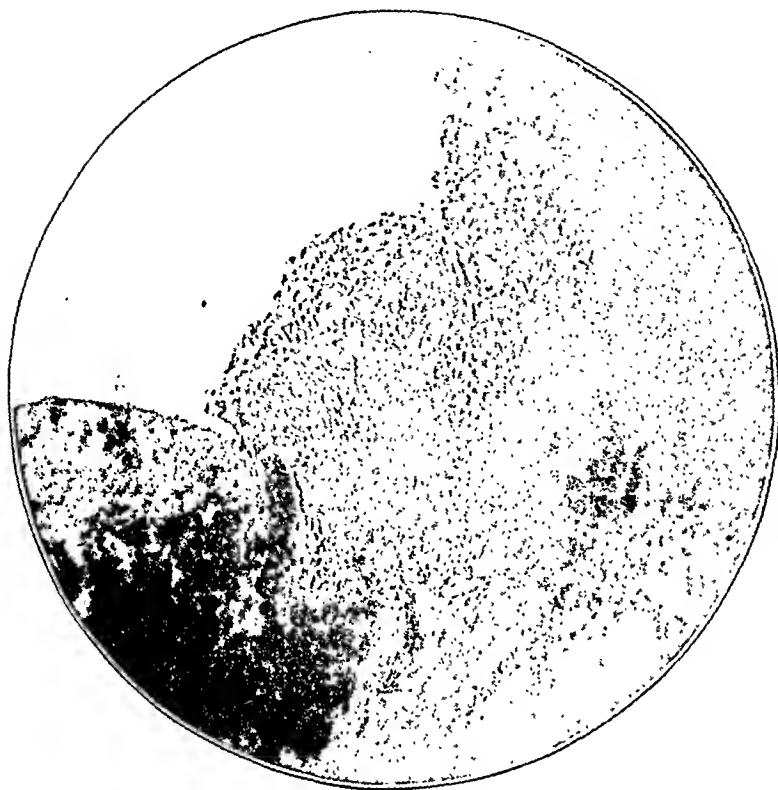
Fig. 3.—Scar tissue in the caruncula. This continues into the scar tissue of the base of the lacus lacrimalis beyond the caruncula.
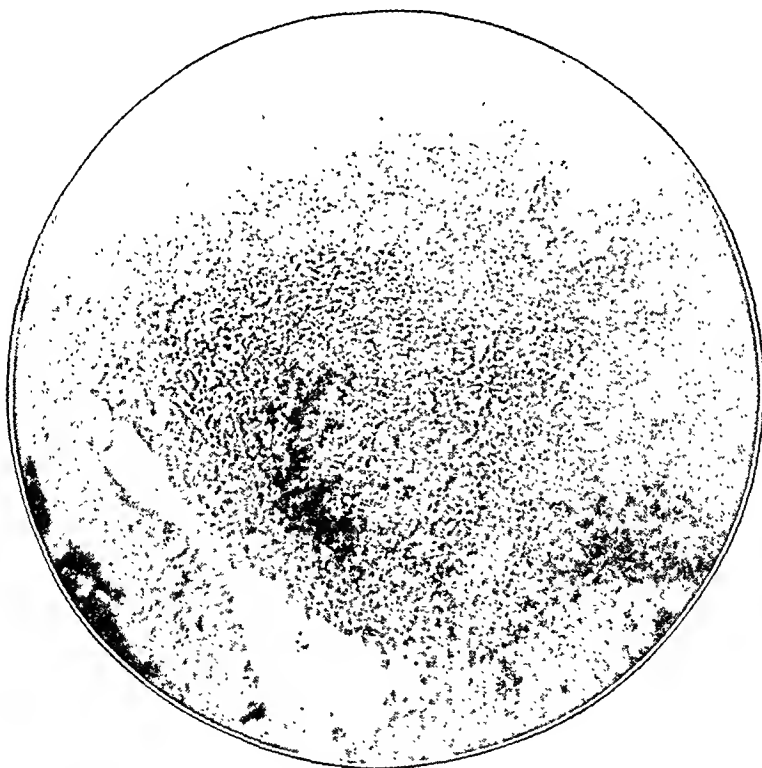
Fig. 4.—Follicle of lymphocytes immediately under the epithelium, surrounded by a capsule of scar tissue.
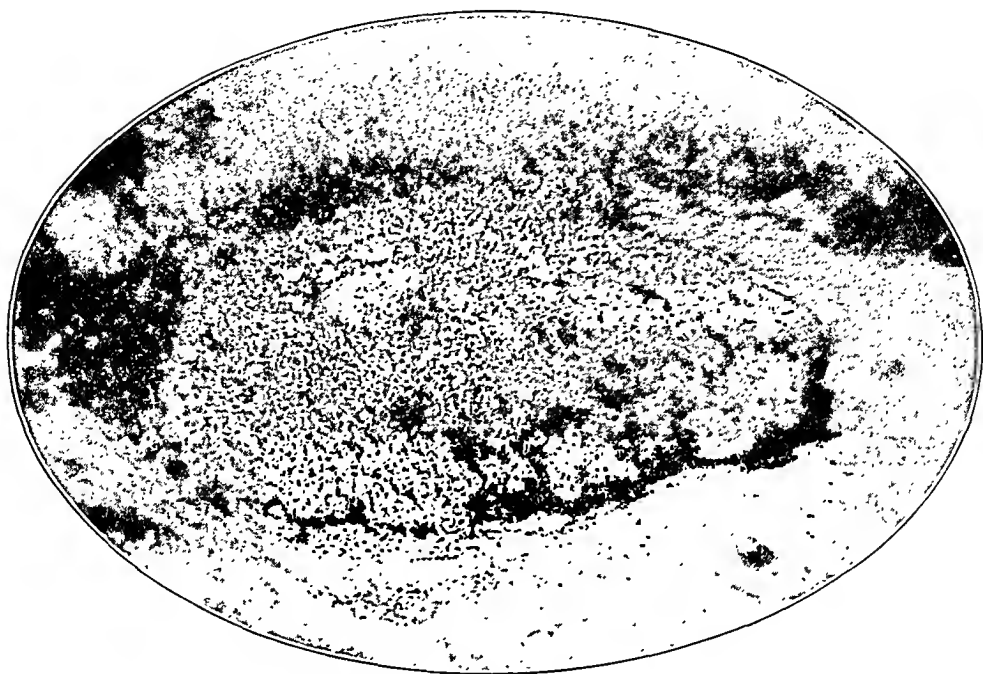
Fig. 5.—Another trachomatous follicle, consisting mainly of lymphocytes and granulation tissue cells. It took a lighter stain than that in figure 4.
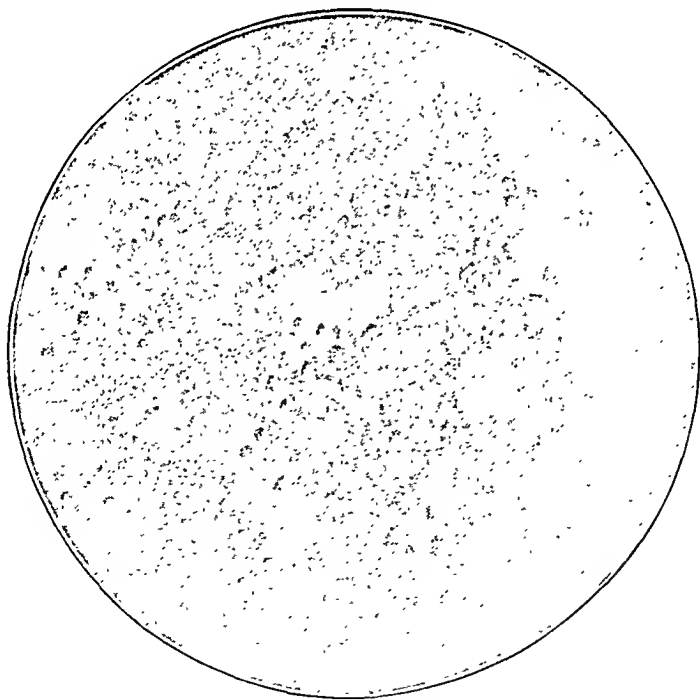
Fig. 6.—Part of one follicle; × 400. Only lymphocytes are visible.
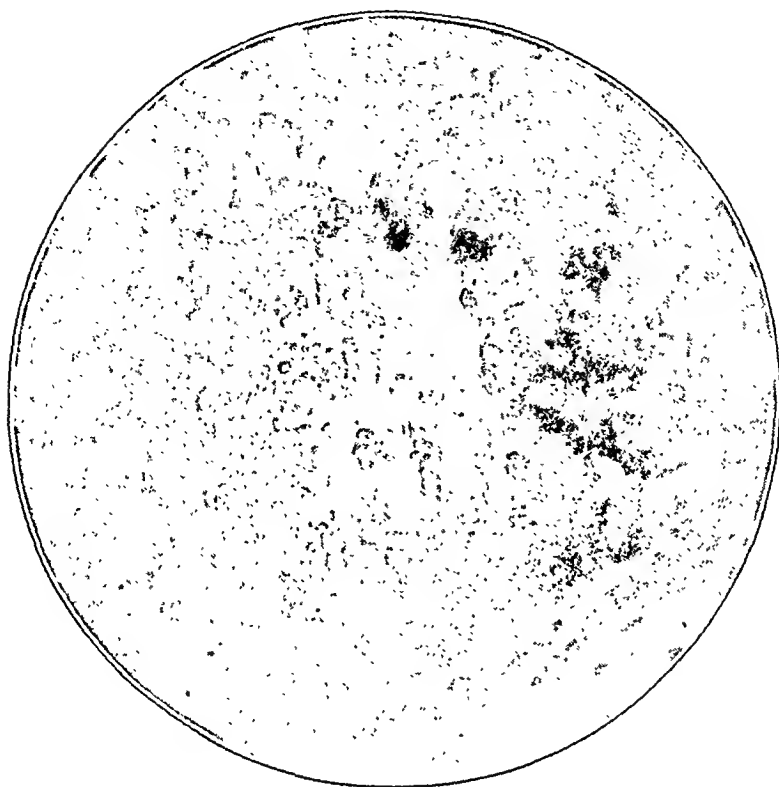
Fig. 7.—Part of another follicle; ✕ 400. Besides the lymphocytes, a cell with lighter and more abundant protoplasm is visible.
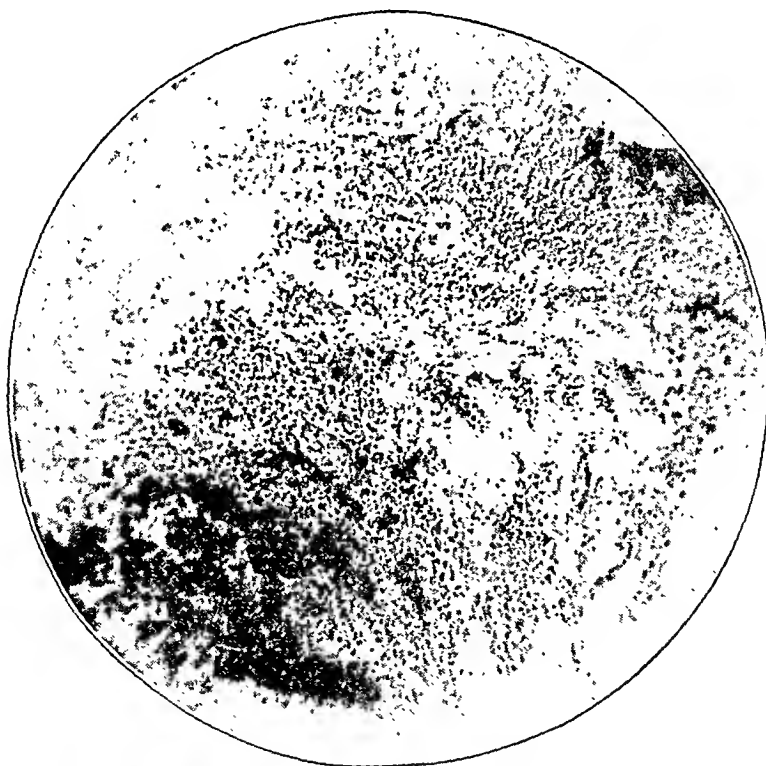
Fig. 8.—Thinning of the epithelium and extensive scar tissue. Fine processes extend from the scar tissue under the epithelium, and between the processes inflammatory infiltration is visible.

Part of one follicle is shown in figure 6. Only lymphocytes are visible.

Part of another follicle is shown in figure 7. In this section, beside the lymphocytes, cells with lighter and more abundant protoplasm were visible; their nuclei were oval and contained a fine chromatin network. The nucleoli were usually easily distinguishable. These cells arranged themselves in small and large groups and could be better detected at low power magnification (fig. 5).

CASE 3.—S. H. had had trachoma for decades and had been treated with drops of silver nitrate for a long time, during which she has been a patient in the psychiatric division of the hospital. Besides an extensive argyrosis, she had a scarred and atrophic conjunctiva. Periodically pannus occurred. The caruncula was atrophied. The fold delimiting the lacus lacrimalis was pulled apart with a hook, but there was nothing notable on the base of the lacus. However, at the site where the caruncula should be, there was a yellow-gray spot, somewhat elongated in the direction of the palpebral fissure.

The epithelium was thinned (fig. 8). There was much scar tissue in the caruncula, from which fine processes extended under the epithelium, and between the processes inflammatory infiltrations were visible.

By summarizing the essential features in the foregoing preparations the pathologic picture of encanthis trachomatosa is obtained.

Under the epithelium of the caruncula, inflammatory infiltration consisting of thick masses of lymphocytes occur. The epithelium, due to the pressure caused by the infiltration, thins by stretching. The inflammatory infiltration is usually without structure. However, typical trachomatous follicles consisting of lymphocytes may be seen under the epithelium; these are surrounded by a capsule of scar tissue. A follicle may show the lighter staining cell of granulation tissue in addition to the lymphocytes, indicating that the scar formation has begun in the follicle itself. The follicles do not have a regular oval form; the follicles under the epithelium are rounded toward the epithelium, but the part toward the medial side of the caruncula is slightly elongated. The follicles within the caruncula are elongated at both ends. The form of a follicle is determined by its environment. This explains why the part of a follicle facing the epithelium is rounded, whereas farther inward, where scar tissue surrounds the follicle, it is compelled to adapt its shape to the location of the scar tissue. Despite the deformity of its outline, it cannot be considered anything but a trachomatous follicle. Scar tissue is found in the caruncula which resembles a finely branched tree. In the main mass of the scar tissue itself no foreign formation is found, only occasional connective tissue cells. The branchlike processes of scar tissue surround a small number of sweat glands, sebaceous glands and hair follicles. When the trachoma is severe the processes branch under the epithelium and are accompanied by inflammatory infiltration. The scar tissue observed in the caruncula is not a formation in itself but is connected with the scar tissue of the lacus lacrimalis. In the root of the caruncula numerous papillae are found

side by side, to the bases of which the processes of the scar tissue can be followed. The processes of scar tissue do not extend into the papillae themselves.

Macroscopically, there frequently is no visible change on the caruncula; sometimes it is swollen and reddened at the beginning of the trachoma. In some cases the caruncula atrophies owing to the general scarification. There is no elevated formation at the base of the lacus; at best it is on level with the lacus itself. The spot where the caruncula used to be indicates by its divergent color the change in the caruncula.

SUMMARY

On the basis of clinical observations, it was assumed that the caruncula plays a part in trachomatous inflammation. Transconjunctival expression of the involved area led to healing in given cases. This, too, supports the foregoing assumption. Pathologic studies of excised specimens support this assumption in every respect. This fact justifies the employment of transconjunctival expression in given suitable cases as the therapeutic procedure insuring the best results.

RESULTS ACHIEVED BY ORTHOPTIC TRAINING IN THE CORRECTION OF STRABISMUS

CLARA BURRI, Ph.D.

CHICAGO

Since the value of orthoptics and its place in the general program of the treatment of squint are still matters for controversy among American ophthalmologists, a report of results obtained from such training over an extended period may aid in placing this method in its proper relation to other methods of treatment for strabismus. It is with this purpose that the following report is presented.

When speaking of orthoptics, not only fusion training is implied but other methods, such as occlusion and the use of atropine, prisms and bifocal lenses, are also included in the concept. In the orthoptic clinic at Northwestern University Medical School usually a combination of these methods is employed. The particular combination employed depends on the specific need of the patient. However, every person receives fusion training with one of the major amblyoscopes or the rotoscope. Exercises are given only once a week, and no home training is expected. Naturally, two or three exercises a week would be preferable, but no facilities exist for such a course of training. But even such weekly exercises have brought beneficial results.

No attempt is made to analyze the material presented in terms of any one method of treatment or in terms of the types of squint, since such analyses were made by others, such as Worth,[1] Pugh,[2] Mayon[3] and Guibor.[4] The aim of this study is to determine the efficiency of orthoptic training in general, as postoperative treatment for persons with squint and as treatment for persons with amblyopia ex anopsia.

It should be noted that all the patients considered in this report who through refraction with a cycloplegic indicated the need for glasses had worn their glasses a variable period prior to entering the clinic and thus had presumably corrected their accommodative difficulty as a causative

1. Worth, C. A.: Squint: Its Causes, Pathology and Treatment, ed. 5, London, Baillière, Tindall & Cox, 1921.

2. Pugh, M.: Brit. J. Ophth. 18:446, 1934.

3. Mayon, L.: Brit. J. Ophth. 19:37, 1935.

4. Guibor, G. P.: Classification of Concomitant Strabismus: Results Secured in Various Types, Arch. Ophth. 19:947 (June) 1938.

factor. Thus, the patients who are reported as recovering from their refractive error alone are naturally almost nil, since that type of patient has not been treated in the clinic.

Only patients with strabismus are considered in this report. Patients with heterophoria will be discussed in a subsequent report. Since in some instances it is difficult to differentiate between a phoria and a squint, the following criterion was adopted: Any person who showed a deviation under cover but who had binocular vision, fusion and stereopsis when the cover test was not applied was considered as having heterophoria, while the patient with some deviation or absence of fusion when binocular vision was not broken up with the cover test was considered as having a squint. Such an apparent deviation can usually be readily observed, except in some borderline cases of small degree or in cases in which the squint becomes only occasionally manifest.

No classification of patients as to types of strabismus is attempted. Whether they had divergent or convergent, monocular or alternating, accommodative or muscular squint, all patients were classified according to their improvement in general. However, careful note was made of existing amblyopia or suppression and the patient's improvement during the period of orthoptic training. Particular emphasis was placed on this because there still exists considerable doubt concerning the extent to which amblyopia can be improved. In general, Continental ophthalmologists report better results in their efforts to overcome amblyopia ex anopsia than do American ophthalmologists. This difference in improvement may be due to the method used; i. e., they first employ total occlusion of the fixing eye, while the latter frequently do not insist on such drastic measures but allow the child to use the good eye a part of the time. But sometimes widely varying results are reported, even after long periods of constant occlusion are employed. Some reports speak of spectacular recoveries, while others show comparatively small changes. Perhaps another reason for this difference in results is due to the fact that in 1 case true amblyopia is being dealt with, and in another, suppression only. Frequently the concept of amblyopia ex anopsia is vague and poorly defined, so that often the reader is uncertain what the author's idea is of amblyopia in considering its relation to strabismus. Again various authors disagree on the standards of visual acuity which constitute amblyopia. Greater care in defining a given concept would frequently eliminate much confusion and misunderstanding and exorbitant claims.

In this study cases in which the corrected vision in one eye is 20/40 or less shall be called cases of amblyopia ex anopsia. Any improvement of the visual acuity subsequent to the initial refraction is considered as improvement of the amblyopia.

The patients considered in this report have been grouped into two divisions for a comparative study. The first group consists of 174 patients who received orthoptic training between 1933 and 1937 and the second group of 82 patients who were receiving orthoptic exercise or who did so during the past two years. All of these patients were seen at the orthoptic clinic of the Northwestern University Medical School. Patients in the first group have become inactive, thus all data for this group were taken from the records made during the period of training. Thus, with these patients no follow-up examination was possible, and therefore no analysis of the results shall be made. The data for this group are presented primarily to show the similarity in the general trend of the results from orthoptic training throughout a period of years. Most of the patients of the second group had a check-up examination sometime during the two months previous to the writing of this report;

TABLE 1.—*Effects of Orthoptic Training on Patients at the Clinic Between 1933 and 1937*

Effect of Orthoptics	Number of Patients
Recovery with glasses alone......................................	1
Recovery with orthoptics alone................................	25
Improvement with orthoptics alone............................	30
Recovery with operation and orthoptics.......................	14
Improvement with operation and orthoptics...................	17
No improvement regardless of the method....................	28
Insufficient record	59
Total..	174

"insufficient record" is used to designate all instances in which no reliable information was obtainable.

The data are classified as follows: recovery with glasses alone; recovery with orthoptic training alone; improvement with orthoptic training alone; recovery with operation and orthoptics; improvement with operation and orthoptics; no improvement whatsoever regardless of which method was used, and insufficient record. For the second group of patients the "no improvement" classification is omitted because careful check was kept on all patients, and as soon as it was noticeable that there was no improvement from orthoptics the patient was referred for operation, and training was continued afterward if any deviation remained or if binocular vision and fusion and stereopsis were defective.

Table 1 shows the various effects of orthoptic training on those patients who attended the clinic between 1933 and 1937. It gives the number of the patients who recovered and improved from orthoptic training and of those who recovered and improved from operation plus orthoptic training. It also shows the number of patients who did not

cooperate sufficiently to get any benefit from training and those who did not improve as a result of the training they received.

Table 2 shows the same thing as table 1, only it contains the data for patients who received orthoptic training during the past two years.

In general, these tables are self explanatory, although a word of explanation should be given as to the criteria of recovery which are used. A patient was considered recovered when the eyes were parallel for near vision and distance, with glasses. In addition, fusion stereopsis and fusion amplitude were required to be present and the ratio between abduction and adduction such as to allow comfort in the use of the eyes in everyday life. This, at least, was the criterion applied to the second group of patients. Since the older patients could not be reached for a check-up examination, this rigid standard could not always be maintained. In those cases a patient was considered recovered if, according

TABLE 2.—*Effects of Orthoptic Training on Patients Treated During the Past Two Years*

Effect of Orthoptics	Number of Patients
Recovery with glasses alone	0
Recovery with orthoptics alone	20
Improvement with orthoptics alone	22
Recovered with orthoptics and operation	8
Improvement with operation and orthoptics	14
Insufficient record	18
Total	82

to the clinic record, his eyes were parallel with glasses and if he had good fusion and stereopsis at the time when tested last.

As has already been explained, the two groups showed the same general tendency. The only marked difference between them is the number who gave insufficient cooperation—those who either came in irregularly or so infrequently that it was impossible to judge the effect of orthoptic training on the basis of their achievements.

In the second group, 20 patients, or one fourth of the group, recovered with orthoptics alone. All of these persons comply to the standard as set up. Four of them maintain fusion and stereopsis and parallel eyes even without glasses. One has been without glasses for the past six months, and the others remove them occasionally for several hours at a time. Most patients who recovered by orthoptic training alone were those whose errors of refraction were a distinct factor. High hypermetropia with the accompanying excess of accommodation and convergence is a well recognized factor in strabismus, and, according to the experience of some ophthalmologists, it is the accommodative squint which most easily can be corrected by orthoptic training. Owing to the importance of the accommodative factors in strabismus, the prognosis

for orthoptic training is best if the squint is greater for near vision than for distance and if it is less with glasses than without glasses. This type of patient may learn to go without glasses eventually.

In most cases the degree of the deviation was low, but some patients recovered who had considerable initial deviation. This may be seen from table 3.

Table 3 shows the degree of the initial deviation of those patients in group 2 who recovered by orthoptic training alone. The degree of squint recorded is with glasses and in terms of prism diopters, as measured with the screen test. The size of the deviation without glasses

TABLE 3.—*Degree of Initial Deviation for Patients in Group 2 Who Recovered From Orthoptic Training Alone*

Patient	Convergent Squint		Divergent Squint	
	Deviation for Near Vision	Deviation for Distance	Deviation for Near Vision	Deviation for Distance
1	40	28	..	..
2	45 3L hyper *	36	..	..
3	20	14	..	..
4	15	5	..	..
5	10	4	..	..
6	20	15	..	..
7	40	20	..	..
8	52 4L hyper	32	..	..
9	6	..	..	12
10	10	5	..	..
11	16	10	..	..
12	..	..	35	55
13	..	..	22	16
14	30	25	..	..
15	10	6	..	..
16	12	..	..	5
17	38	35	..	..
18	14	8	..	..
19	16	10	..	..
20	20	10	..	..

* "3L hyper" signifies a vertical deviation, making the squint more complex.

is not reported because the general picture would be very similar, the only difference being that the degree of the variation is larger. This is the case except for a few patients for whom the correction of the refractive error did not affect the degree of the strabismus. This would indicate that even if squint is not primarily of the accommodative type, orthoptic training may be of aid in correcting it.

If orthoptic training causes no improvement or if improvement stops, the patient is referred for operation. If, after operation the eyes are not parallel or if fusion and stereopsis are not present, the patient again receives training. For this study the patients who were operated on are considered from the point of view of postoperative training regardless of what treatment they had received prior to the surgical procedure. The data are found on lines 4 and 5 in tables 1 and 2. Thus, under

recovery with operation and orthoptics and improvement with operation and orthoptics are enumerated those patients who received fusion training or any other orthoptic measures after operation, although most of these patients had some orthoptic training before operation. Of these persons, 14 in the first group recovered and 8 in the second group, and 17 in the first group improved and 14 in the second group. Since most of the patients of group 2 are still receiving training, some who are classified as having improved may later recover should they continue their exercises. Of those who recovered with operation and orthoptics, only 1 patient has parallel eyes without glasses, except those who never needed glasses.

The notation "insufficient record" in the second table includes not only the records for those who did not cooperate but also for those who entered training too recently to show any results. Four of these 18 patients entered the clinic only a month before this report was written. Two will probably need to be operated on because they have a large

TABLE 4.—*Effect of Orthoptics on Amblyopia*

	Group 1	Group 2
Total number	85	33
Number improved	23	19

deviation. If there is no stimulation or desire for fusion, there is little hope for the development of binocular vision. This would be with deviations as high as 40 to 50 arc degrees. Until the deviation has decreased by operation so as to bring the eyes into an approximate position of parallelism where training can become effective, functional training is of little use, or at least gives only slow results.

Table 4 shows the effect of orthoptics on amblyopia or suppression. The number of patients who gained in visual acuity seems similar in the two groups. However, this similarity is only apparent. In terms of percentage, the second group did gain more, but even this greater percentage may be an artefact. Many of the 59 patients in group 1 who did not cooperate sufficiently enough to have any results recorded had poor vision in one eye, which, had they received training, might have improved. Since all these records are included for the total number of patients with amblyopia for the group, and since the total number of patients who did not cooperate is so much larger in group 1 than in the other group, the data from this should not be considered as directly comparable.

In general, the improvement in visual acuity was not spectacular. Only 1 patient made a quick recovery, a girl whose visual acuity in the

left eye improved from 20/200 to 20/30 in about three weeks of total occlusion. She had a hyperopic correction in the fixing eye and a myopic correction in the amblyopic eye. When she first came to the clinic she did not wear glasses, although after refraction the minus lens apparently did not improve the vision in her left eye even after wearing it for a week. After occluding the good eye, the myopic eye learned to respond to the corrective lens. After occlusion was discontinued, however, the visual acuity again diminished. It was only after the patient learned to fuse and after some binocular vision had been developed that the visual acuity remained improved. Perhaps many of the so-called quick recoveries which are reported in sales promotions for orthoptic instruments are of similar nature. All the other patients in this study who showed improvement in visual acuity did so slowly. Also, the amount of improvement was variable and probably depended partly on the length of occlusion, the regularity of occlusion and the age of the patient.

Of the patients who showed improvement in visual acuity, 2 gained 4 lines on the Snellen test chart; 1, 3; 11, 2, and 5, 1. Most of the increase in visual acuity, in terms of both frequency and degree of improvement, occurred in patients below the age of 10. Nine of the amblyopic group who improved were less than 10 years old, 3 between 15 and 20, 3 between 20 and 25 and 1 older than 25. All those who gained 4 and 3 lines were below the age of 15. The older ones gained only 1 or 2 lines. Chronologic age is undoubtedly a factor in determining the amount of improvement, but the fact that older patients cannot always carry out regular occlusion of the good eye should also be considered as a possible explanation. This would especially be true if the poorer eye has too low a visual acuity for them to carry on with their daily activities.

Another question which may be raised by a critical reader is: Why do some patients with amblyopia ex anopsia improve while others remain the same in spite of occlusion and fusion training? Some patients seem to learn to fuse large objects with as little as 20/200 vision in the poor eye, and many get fair fusion, although little stereopsis, with 20/65, and with 20/40 little should stand in their way toward good binocular vision. Although some actually acquire binocular vision in spite of definite amblyopia, still their vision does not improve. What causes the difference?

Wherein lies the difference between the 35 who remained the same and the 18 who improved, however little this may have been? Better cooperation, no doubt, is part of the answer for some and the whole answer for others. However, some patients with low visual acuity will not improve even if their eyes are occluded constantly for weeks and

months. Perhaps the clue to the problem can be taken from the case described at first. Could it be that in some cases one is dealing with suppression and not with true amblyopia? Perhaps these are two different kinds of low acuity rather than one kind of varying degree. This certainly would explain why in some cases even constant occlusion gives such poor results.

By way of recapitulation, the following points may be emphasized: Orthoptic training as employed at Northwestern University Medical School has definite merit in the treatment of squint. Although only weekly exercises were administered, one fourth of the patients treated during the past two years recovered with orthoptic training alone and another fourth improved more or less, depending on the degree and complexity of their squint and the duration of the total time during which they received training. Accommodative strabismus has the best prognosis for complete recovery from orthoptic exercises alone. However, orthoptic training should not be regarded as a technic for a cure-all, but rather it should be valued as an aid to operation, both before operation and for correcting any remaining deviation or defect in fusion and stereopsis after operation has been done. For example, of the patients included in this study, another fourth either recovered or improved with the aid of functional training after operation failed to correct their deviation completely. Even though operation may bring about parallelism, it seldom gives binocular vision and good fusion, and it is here that functional training can make its unique contribution. Experience will undoubtedly show that an intelligent selecting and combining of the two methods will bring about much better and more permanent results, both cosmetically and functionally. It is with orthoptic training that good binocular vision, good fusion and stereopsis can be brought about and maintained. One is also impressed with the lack of cooperation which a large percentage of the patients have shown. In order to evaluate the benefits achieved from orthoptic training, the clinic at Northwestern University has established a policy whereby an explanation is made to the patient as to the importance of following the recommendations in detail. Patients who are unwilling to do this are not encouraged to enter the clinic for orthoptic training.

Dr. Sanford R. Gifford and Dr. George E. Park offered opinions, observations and helpful suggestions which aided in the preparation of this report.

LINES ON THE BULBUS BENEATH THE CONJUNCTIVA

EMIL OLÁH, M.D.

Chief Ophthalmologist, State Hospital

GYULA, HUNGARY

If the upper palpebra is pushed loosely upward and backward with a suitable instrument [1] which follows the curvature of the bulb while the person examined looks downward, in some instances easily distinguishable lines can be seen macroscopically under the conjunctiva. These lines, depending on the illumination, can usually be discerned best from the front, but sometimes they can be seen only from the side. In many instances they can be seen only in a dark room with focal lighting, but at times they are not visible even under these circumstances. In the dark room also they are best seen from the front, but at times they are visible only from the side. Their number is variable. From two to seven lines were noted in the eyes examined at the Hungarian State Hospital. The larger the number of the lines observed, the more evident does their meridional arrangement become. The lines which run toward the conjunctival fornix are 3 mm. apart, and those that run toward the cornea are 2 mm. and even less apart. This meridional arrangement is less distinct if only two such lines are visible; in such instances the course of the lines appears to be parallel. The lines can be followed toward the fornix as far as the upward displacement of the palpebrum permits. It is notable that the lines running toward the cornea rarely reach the limbus. They usually cease within a few millimeters of it. Very rarely an oblique line is observed between two meridional lines, but it disappears before it connects them.

Frequently there seem to be impressions on the surface of the conjunctiva corresponding to the lines, as if there were real grooves. However, careful examination from all sides shows that there are no such grooves. This false impression is caused by the fact that the lines sometimes are of a different shade from that of their surroundings; frequently it is found that their color is no different from that of the

neighboring structure but that there are two streaks of brightness along the sides of each line which cause this difference. The streaks are hardly wider than the lines themselves and direct attention to them. If such streaks are visible, the lines, too, are sure to be found. The bulbar conjunctiva is transparent, and with a binocular loupe or a slit lamp the superficial and deep conjunctival vessels can be seen to pass above the lines; therefore, the lines are beneath the deep conjunctival vessels. The transparent conjunctiva has its own refractive surface, and this is different directly above a line and along the side. The refractive surface on each side of a line must be identical, because if it were not one would observe a bright streak only on one side of a line and not on the other. These streaks of brightness do not follow a line along its entire course but in places break into numerous parts on one side of the line and not on the other. Their position varies according to the movements of the eye.
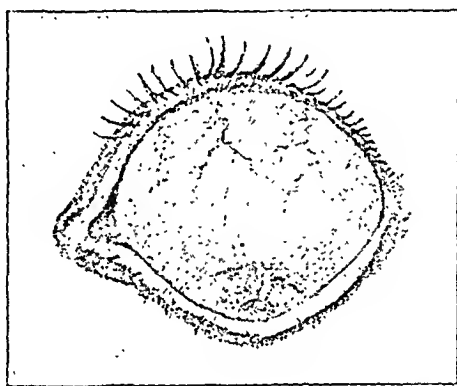
Subconjunctival lines on the bulb.

These lines can be observed only in the area of the bulbar conjunctiva superior to the cornea. Repeated examination of an eye always shows the lines in the same formation.

However distinct these lines may be, they easily become invisible. If the person examined looks downward and the eyeball is gently massaged through the upper palpebra, the lines cannot be seen. In most cases eversion of the upper palpebra with the finger or with a spoon is sufficient to cause them to disappear. This manipulation causes the eye to become red without becoming any more vascular. The mesh of fine capillaries is filled with more blood than is present normally, and this destroys the transparency of the conjunctiva in addition to changing the refractive conditions. If a drop of epinephrine hydrochloride is instilled under the upper palpebra to prevent the distention of the capillaries with blood consequent to the massage, the subconjunctival lines can be seen as well before as after massage.

If the person examined looks downward and moderate pressure is applied through the upper lid, the instrument being moved sidewise, it is seen that the end of the line near the fornix moves in the same direction and degree as that in which the instrument itself was moved. This deflection of the line occurs in only about one third of its extent, the part nearest the fornix.

At the series of examinations made at the Hungarian State Hospital the lines were rarely observed at first because they were sought for by direct inspection; however, later, when lateral inspection was employed, they were observed far more frequently. They may be seen more often in a dark room with a binocular loupe, but in such instances the bright streaks accompanying the lines cannot be observed in their characteristic form. In many cases the lines can be made visible in the upper half of the bulb (even if they cannot be seen macroscopically or with the binocular loupe) by exercising moderate pressure on the lid, which is pushed upward and backward. The lines cannot be made visible in the lower half of the eyeball by the application of pressure. It has also been observed that in the same person the subconjunctival lines can be seen well in one eye but in the other eye can be seen only after the use of pressure and frequently not then. These lines were never observed in children or in the cadaver, not even with the aid of the described technic.

The explanation for the presence of these subconjunctival lines is to be sought for in the histologic structure of the eye; however, it is possible that the explanation can be made only on physiologic grounds. Histologic study of the lines was made by Dr. Karoliny, director of the pathologic department of the hospital. He will publish his results separately.

A question which must be answered before one considers the results of the histologic examination pertains to the possibility of the lines being artificial products. The examiner must determine whether they are due to his own manipulation.

The idea that the lines might be artificial products arose because in many cases lines which were otherwise invisible were made visible in a dark room with focal illumination by means of mild pressure on the eyeball through the upper eyelid in a line parallel with the limbus, the lid having been pushed upward and backward. Therefore, in those cases in which the lines were not visible except after pressure, the question arose as to whether they were not artificially produced.

Besides the observation that in certain cases these lines can be made visible, there is not a single other observation on which to base the assumption that they are due to an increase of tension in the conjunctiva produced by the subject's downward gaze and the displacement of the

lid upward and backward. On the other hand, numerous facts can be listed as indubitable proofs that these lines cannot be considered artificial products. They appear even before the patient has directed his gaze completely downward and before there is any tension on the conjunctiva; as a matter of fact, when requested, the subject can look even more obliquely downward. However, if the lines were caused by tension, the traces of tension would appear wherever the conjunctiva is under tension and not at intervals of a few millimeters, as lines. But these lines appear when the lid is pulled up with the finger or with the aid of some specially constructed spoon. Desmarres', Brana's and Oláh and Keppich's spoons were used in the studies referred to here. It has also been observed that if the same subject is examined on several occasions and if the subconjunctival lines can be seen macroscopically on only one of the eyes with the aid of some spoon, these lines can be detected macroscopically without the spoon only on that eye on which they were repeatedly observed previously and not on the other eye. In addition to meridional lines, occasional oblique lines have been observed. With upward displacement of the lid, the tension of the bulbar conjunctiva can be only meridional in direction, and under no circumstance can it produce lines of an oblique course. The lines were observed in the upper half of the optic bulb and were never seen or produced in the lower half. They were most frequently seen around 12 o'clock (clockwise). If a person is examined in whom it has been noted that these lines are distinctly visible on occasion and if the downward gazing eye is massaged through the upper lid, the lines cannot be made visible. If, however, the conjunctiva is avascularized previously by instillation of drops of epinephrine hydrochloride under the upper lid, the lines become visible after massage. If an area in which the superficial and deep conjunctival vessels meet above a subconjunctival line can be brought into focus by the aid of the slit lamp or the binocular loupe, it is clearly visible that the lines do not extend through the entire thickness of the conjunctiva but are located under the deep conjunctival vessels. If these lines were the product of tension, then the tension would leave traces of its existence everywhere, but especially on the conjunctiva. In these cases it is evident that the lines are under the deep conjunctival vessels.

On the basis of these observations, it is concluded that these subconjunctival lines cannot be considered artificial products of manipulation.

Clinical Notes

OCULAR TRANSILLUMINATORS

BENJAMIN FRIEDMAN, M.D., NEW YORK

After experimenting for a considerable time with transilluminators made of plastic materials, I have come to the conclusion that the most practical method of delivering the brightest possible light at the point of illumination is one by which the light source is in direct apposition to the eye. The accompanying illustration depicts a pair of transilluminators
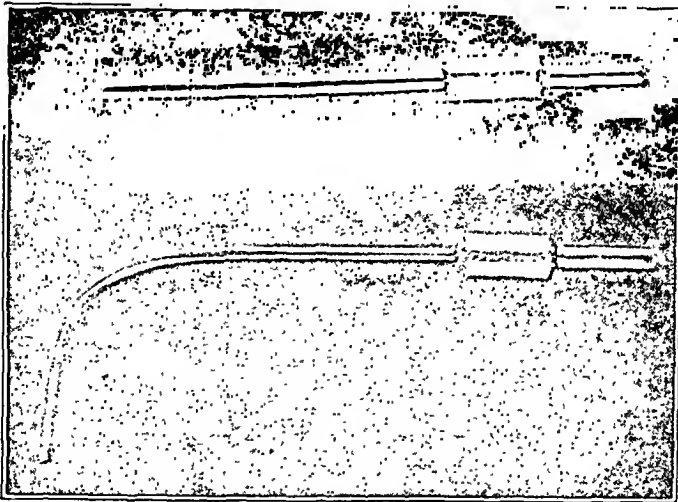
Ocular transilluminators.

which I have found to be effective. They are adapted to fit into the handle of the standard ophthalmoscope and carry a tiny 2 volt bulb at the tip.

A straight model is employed for transillumination of the anterior segment of the eye and a curved form for retrobulbar transillumination. The straight transilluminator has a post 6 cm. in length and 3 mm. in diameter. The end tapers flush with the bulb, so that only 1.25 mm. of the curved glass is exposed. The diameter of the bulb at this level is only 2 mm. The part in contact with the tissues is rounded and presents a minimum of surface. The disturbing lateral dispersion of light is reduced to a minimum.

The curved model is somewhat thinner in diameter, being 2.5 mm. at its widest part. An oval window is cut as near the tip as is practicable, facing the eye. The window measures 1.5 by 1 mm. The bulbs are replaceable at a cost similar to that of the ordinary ophthalmoscope bulb.

There is nothing particularly original in either the idea or the form of the transilluminators. I have merely attempted to simplify the design and reduce the cost as much as possible.

All the credit for whatever value the instruments possess must fall to the painstaking precision work of the instrument maker.[1]

1. The instruments were made for me by J. Brandenberg & Co., New York.

A QUICK METHOD FOR SHARPENING OCULAR TREPHINES

MARSHALL STEWART, M.D., BROOKLYN

The necessity for a sharp trephine in performing the Elliot sclero-corneal trephining for glaucoma is undebatable. A mounted dental Arkansas stone can be obtained from a dental supply house or a dentist.
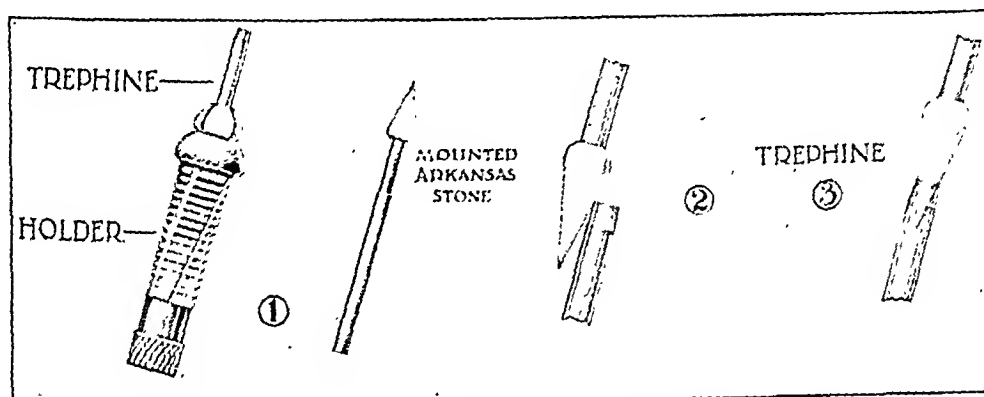
Material and technic for sharpening ocular trephines.

A wet mounted stone, as shown in *1* of the accompanying illustration, is placed in the rotary chuck of a dental engine and sharpened in a circumferential manner on the outside beveled portion of the trephine, as shown in *2*. The full amount of sharpening should be done on the outer beveled portion. The wire edge is removed by a light circumferential reaming on the inside of the trephine, as shown in *3*. The revolving stone should not be forced down to occlude the trephine opening, as the stone will "jam." Caution should also be observed not to produce an internal bevel or "cornucopia" effect. This condition might cause a serious complication should the sclerocorneal plug drop into the anterior chamber. The smaller the bore of the trephine the greater should be the degree of sharpness, because of increased tortion of the tissue plug, owing to a relatively longer plug.

If the operator cannot obtain an Arkansas mounted dental stone, a carborundum stone can be used. Carborundum is not as satisfactory because of pitting of the stone while in use. The Arkansas mounted stones were originally used for burnishing the old-fashioned "hammered in" dental gold fillings and were formerly seen in barber shops as a

marble gray razor hone. To the operator who works in a "budgeted hospital" or in a locality where a sharp trephine is not available, this method is very satisfactory.

A DIAGNOSTIC CONTACT LENS MADE OF LUCITE

Otto Barkan, M.D., San Francisco

Owing to an increase in popularity of gonioscopy, a demand has been created for a less expensive diagnostic contact glass. Following Dr. Jonas S. Friedenwald's suggestion, Gradle [1] constructed a diagnostic contact lens made of lucite [2] which he demonstrated at the meeting of the American Ophthalmological Society in San Francisco in
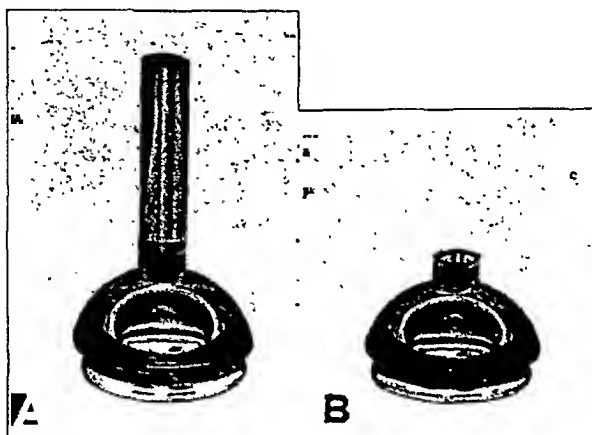
A, lucite contact glass with a small detachable handle which facilitates holding the lens in position. *B*, lucite contact glass with the handle detached.

June 1938. I had at that time constructed a molded contact glass of lucite [3] which has characteristics and optical principles similar to those of the Koeppe glass and different from those of the Gradle lens. The stemlike feature of the latter was incorporated as a detachable handle in order to add to its convenience.

The present lens, shown in the accompanying illustration, is used in the examination of the anterior chamber angle in the same manner as the regular Koeppe lens. This lens has an inherent magnification of $\times 1\frac{1}{2}$. This means that 50 per cent more magnification is added to that furnished by the loupe or corneal microscope. The lens may be cold sterilized but must be carefully dried, since lucite is softer than glass and its surface may become marred with scratches. The cost of the lucite lens is only a fraction of the cost of a glass lens made for the same purpose.

490 Post Street.

1. Gradle, H. S.: A Contact Glass for Gonioscopy, Tr. Am. Ophth. Soc. **36:** 279, 1938.

2. Lucite is a du Pont product (methyl-metharcylate).

3. The lens may be obtained from Trainor and Parson, 228 Post Street, San Francisco.

TEMPORARY MYOPIA DUE TO SULFANILAMIDE

J. H. Bristow, M.D., Monroe, Wis.

Ocular manifestations of toxicity of sulfanilamide, though rare, are alarming. To find that one's visual acuity is reduced from 20/15 to 20/300 in a few hours is nothing short of a calamity for the patient and the source of no end of anxiety for the physician prescribing the drug. The usual toxic manifestations of the drug and its derivatives are well known and looked for by all physicians prescribing this medication and will not be reiterated here.

Ocular manifestations of toxicity of sulfanilamide have been reported on several occasions, although the pathologic process has usually been confined to inflammatory reactions of the lids and conjunctiva and, in the case reported by Bucy,[1] of the optic nerve. Spellberg[2] has reported a case which in some respects parallels the case reported here, although the pathologic process produced was of a different type. That the etiologic factor of the condition produced is a sensitization to sulfanilamide cannot be denied if the details of the following case are studied. The pathologic process present is apparently an edema of the lens, particularly in its anteroposterior diameter, producing a shortening of the focal length of the lens or, in other words, a myopic eye. A change in the refractive index of the aqueous, lens substance or vitreous due to the presence of the drug in these media need not be considered as a cause of the myopia, as an equal concentration must have been present at the time of the first course of treatment when there was no evidence of myopia. The possibility of a spasm of the ciliary muscle producing an artificial myopia is precluded by the fact that the results of objective and subjective refraction were practically the same before and after cycloplegia was induced. A perfect view of the fundus was obtained throughout the entire period of disability and showed no evidence of pathologic involvement of the nerve head, retina or retinal vessels. The sudden onset of the myopia, due, presumably, to the rapid swelling of the lens, parallels the occurrence of the angioneurotic edema found in other allergic states. The following case history demonstrates an unusual condition produced by a sensitization to one of the most commonly used drugs today.

REPORT OF A CASE

Mrs. K. B. first consulted her family physician on Feb. 1, 1940, at which time she complained of burning on urination and frequency. This was her first attack of cystitis. Physical examination revealed a well developed, intelligent, white woman, 21 years of age and weighing 120 pounds (54 Kg.). Urinalysis at the time of her first visit showed 15 cells per high power field from an uncentrifuged specimen. She was given sulfanilamide, 15 grains (0.97 Gm.), every six hours. On February 3 the symptoms of cystitis had subsided, and there were a few pus

From the Monroe Clinic.

1. Bucy, P. C.: Toxic Optic Neuritis Resulting from Sulfanilamide, J. A. M. A. **109**:1005 (Sept. 25) 1937.

2. Spellberg, M. A.: Toxicity of Sulfanilamide: Severe Transient Myopia Following Use of Sulfanilamide, Illinois M. J. **75**:366 (April) 1939.

cells per high power field. At this time she complained of malaise. She was told
to continue the sulfanilamide for two days and to return. On February 5 urinalysis
gave negative results, and the administration of the sulfanilamide was discontinued.
On February 8 the patient complained of numbness and tingling of the feet and
insomnia. She felt very tired. The white blood cell count at this time was 2,550,
and the Schilling count was normal. The urine was normal. On February 10 the
white cell count had increased to 5,550. On March 2 there was a recurrence of
the cystitis, and the urine contained 15 to 20 pus cells per high power field. The
white cell count at this time was 7,350. Owing to the patient's apparent idiosyn-
crasy to sulfanilamide following her first attack of cystitis, she was given
azosulfamide (neoprontosil; disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-
hydroxynaphthalene-3',6'-disulfonate), 10 grains (0.65 Gm.), every six hours. She
took six tablets on March 2. The next morning symptoms of nausea and dizziness
developed, with extreme lassitude and marked blurring of distant vision.

    Ophthalmoscopic examination at this time showed a clear cornea, an anterior
chamber of normal depth, no iritis and a clear vitreous. Examination of the fundi
revealed no evidence of pathologic involvement of the retinas, retinal vessels or
optic nerve heads. Subjective refraction revealed visual acuity of 20/300 in each
eye without correction. The use of a — 2.00 sphere combined with a — 50 cylinder
at axis 90 in the right eye gave vision of 20/15, and a — 3.00 sphere combined with
a — 25 cylinder at axis 145 over the left eye gave visual acuity of 20/15. Muscle
balance was normal.

    With cycloplegia, the refraction was found to be exactly the same objectively
and subjectively as it was with the manifest method. The patient was again seen on
March 4, at which time her white cell count was 6,400. On March 5 the count
had dropped to 3,250. On March 8 the urine was normal, and the patient had no
cystitis. On March 21 the white cell count was 4,050, and the patient experienced
no untoward symptoms. Her visual acuity was 20/15 in each eye without correction.
Ophthalmoscopic examination revealed no evidence of a pathologic process in the
eyes.

    The patient has been seen on several occasions since and has no apparent
difficulty as the result of her transient myopia.

BITEMPORAL   HEMIANOPIA   OF   TRAUMATIC   ORIGIN

JOHN   W.   HENDERSON,   M.D.
Fellow in Ophthalmology, the Mayo Foundation
AND
C.   WILBUR   RUCKER,   M.D.
ROCHESTER,   MINN.

    Bitemporal hemianopia is an infrequent result of injury to the head.
Østerberg,[1] in reviewing the 30 such cases in the literature and 2 of his
own, found in most of them certain common features: Blunt violence

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    1. Østerberg, G.: Traumatic Bitemporal Hemianopia (Sagittal Tearing of
the Optic Chiasma), Acta ophth. **16**:466-474, 1938.

applied to the front of the skull caused a relatively slight fracture that did not extend to the region of the sella turcica but caused a rupture of the skull cap; the patients were comparatively young men of about 30 years whose skull bones consequently were rather plastic.

The following case supports Østerberg's impressions.

REPORT OF A CASE

A man aged 37 entered the Mayo Clinic on Oct. 31, 1939 complaining of limited fields of vision and of nonunion of a fracture of the left hip. He related that on March 14, 1938, while driving an automobile he had had a head-on collision with a truck. After this accident he had been unconscious for two weeks. On regaining consciousness he noted diplopia and an inability to see in the temporal fields. Within a month the diplopia disappeared, but ever since he had felt as if he were

V. O. S.: 6/30   V. O. D.: 6/7

----- 3/330 white

——— 35/330 white
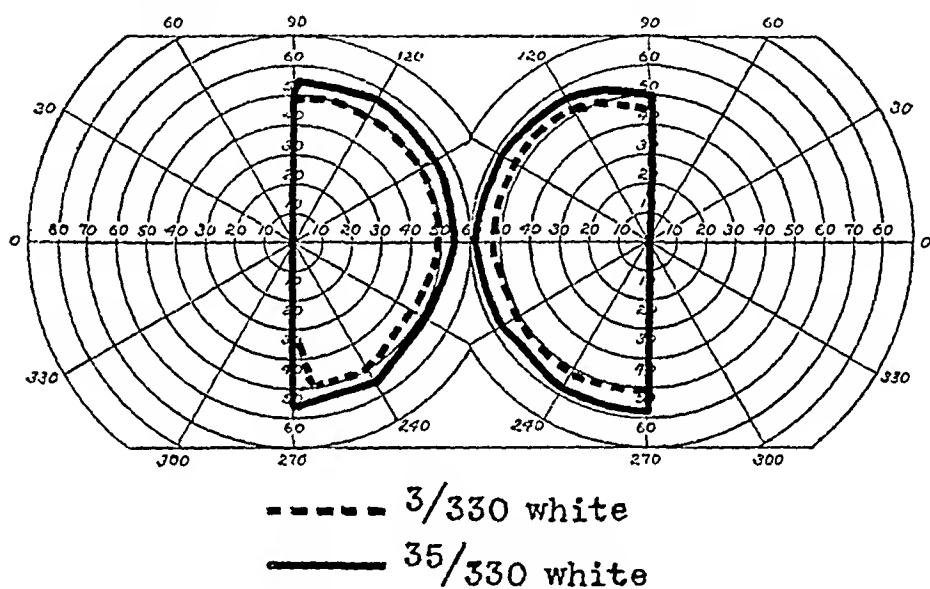
Complete and absolute bilateral hemianopia as revealed by examination of the visual fields.

wearing blinders. His physician had told him that he was suffering from a fracture of the skull and a fracture of the left hip. A Smith-Petersen nail had been inserted in the left femur in an attempt to promote union of the bones around the hip. Examination at the clinic a year later revealed a nonunited fracture of the left hip.

Visual acuity was 6/7 in the right eye and 6/30 in the left. The ocular rotations were normal. The pupils reacted promptly on convergence and somewhat sluggishly to light. Ophthalmoscopic examination disclosed a moderate pallor of both optic disks, the left being slightly paler than the right, with a little loss of substance. Perivascular sheathing around the blood vessels at the margin of the optic disks suggested the presence of a previous papilledema. Examination of the visual fields demonstrated complete and absolute bitemporal hemianopia, as shown in the accompanying chart. There was a midline splitting of the fixation area in the field for the right eye, and in the field for the left eye there was a slight involvement of the macular area within the remaining nasal field. The defects in the visual fields indicated an interruption of all the crossing fibers at the optic chiasm

On neurologic examination anosmia was found. Roentgenograms of the skull and head were considered to reveal nothing abnormal except for some osteomatous thickening around the lateral margin of the left frontal sinus and a small osteoma along the medial wall of the right frontal sinus. This marked the site of the previous fracture of the frontal bones. There was no evidence of a fracture through the base of the skull. One of the orthopedic surgeons removed the Smith-Petersen nail from the left hip and performed transtrochanteric osteotomy of the left hip. The patient was discharged on Nov. 23, 1939, with satisfactory union of the bones of the hip.

There is no convincing evidence of the manner in which fibers in the chiasm are interrupted by fractures of the front of the calvaria. After abstracting the reported cases and adding 3 of their own, Traquair, Dott and Russell [2] suggested that the mechanism may be dependent on rupture of some of the blood vessels of the chiasm followed by local thrombosis and softening. Østerberg pointed out that there are no anatomic grounds for supposing that the central portion of the chiasm has its own separate blood supply, and he posed the question of why the crossing fibers exclusively should be put out of action by a lesion of the chiasmal vessels. After experiments in which he stretched normal chiasms removed at necropsy, he found that multiple minute tearings occurred in the crossing bundles, whereas the noncrossing bundles were spared. He expressed the belief that in some fractures of the frontal bones the brain may be suddenly and violently displaced enough to cause similar lacerations in the chiasm and consequent bitemporal hemianopia.

2. Traquair, H. M.; Dott, N. M., and Russell, W. R.: Traumatic Lesions of the Optic Chiasma, Brain **58**:398-411 (Sept.) 1935.

Ophthalmologic Reviews

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ALLERGIC PHENOMENA IN OPHTHALMOLOGY

ALFRED APPELBAUM, M.D.

NEW YORK

Allergy, as it is understood today, may involve a variety of tissues throughout the organism. Nearly all the tissues of the eye are susceptible to allergic manifestations. Unlike other pathologic conditions which leave definite structural changes to be studied post mortem, the changes in allergic conditions are transient and reversible. A great percentage of patients who present ocular allergic manifestations also present extra-ocular manifestations. An allergic state may color the symptoms of a nonallergic disease.

The eye participates in the general hypersensitivity of the organism, and the ocular lesion is but a single expression of the peculiar body reaction. In order to understand better the variety of ophthalmologic conditions which have an allergic basis, it is not amiss to survey the allergic state before bringing these to the attention of the ophthalmologist.

Thirty-seven years ago, von Pirquet and Schick[1] introduced to the medical world the term "allergy," which they used to denote the altered reaction produced by the first and second inoculations of cowpox virus. Originally, von Pirquet defined allergy as a "changed capacity to react to foreign substance"—an abnormal response to certain extrinsic stimuli—and in his writings he expressed the belief that the basis of the phenomenon was an "antigen-antibody" reaction. Subsequently, Doerr[2] extended this definition to include all forms of changed reactivity, irrespective of whether an antigen-antibody reaction could be demonstrated.

Actually, allergy is a hypersensitiveness of the tissue cells to allergens—a class of substances which give rise to specific alteration in the reaction capacity of the tissue cells when administered to the animal body in a manner excluding their digestive disintegration. Technically, allergens are distinguished from true antigens only in that they do not

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1. von Pirquet, C., and Schick, B.: Wien. klin. Wchnschr. **16**:758, 1903.

2. Doerr, R., in Kraus, R., and Levaditi, C.: Handbuch der Technik und Methodik der Immunitätsforschung, Jena, 1909, vol. 2, p. 856.

appear to cause the production of true antibodies according to the usual laboratory technic, although the mechanism for producing reaction in human beings is probably the same. But there is something in the blood which does react with the allergen. This is demonstrated by the phenomenon of Prausnitz and Küstner. Since this substance is not a true precipitin, it has been termed "reagen" to indicate an as yet unidentified and unisolated substance which reacts with the allergen. The allergic "antigen-antibody" reaction might therefore be better termed today as an "allergen-reagen" reaction.

Every true allergen is believed to be a protein. The group includes not only all known proteins which are soluble in the animal body and chemically foreign to its basic tissue and plasma protein but possibly some of the higher protein split products and protein-lipoid combinations.

After the initial reaction of immunity has passed off and the organism has apparently returned to normalcy, in some instances antibodies remain attached to the tissue cells and "sensitize" them. It is these antibodies which are responsible for the altered capacity to react to foreign substance and initiate the allergic reaction when the "sensitized" cells subsequently are confronted with the same allergen. There is therefore substantial reason to believe that hypersensitiveness in the allergic person depends on previous contact with the particular foreign substance.

The concept of the mechanism involved presupposes the existence of antibodies within the cells proper as well as in the circulation. When the circulating antibodies are present in sufficient concentration to engage the antigen and thus protect the fixed cellular antibodies, the reaction (immunity) takes place unnoticed. On the other hand, when the circulating antibodies are insufficient to offer the fixed cellular antibodies this protection, the antigen-antibody reaction takes place in the cells. In the latter case, the biochemical reaction liberates a histamine-like substance. The cells suffer a certain amount of damage or destruction. There is capillary dilatation from secondary stimulation of the vasomotor system accompanied by increased permeability of the vessel walls, exudation of serum containing toxins and a local necrotizing inflammation (allergic inflammation). Should the antigen-antibody reaction be extensive and severe, the liberation of histamine reaches a great height, and a general musculospasmodic reaction (anaphylaxis) follows. The overproduction of histamine and the consequent dilatation of the arterioles disturb the normal balance maintained by the vascular system and lowers the blood pressure. Immunity, allergy and anaphylaxis, then, are closely related to one another, differing only quantitatively. Progress in clinical allergy has been based on knowledge of the phenomena of experimental anaphylaxis.

In 1903 Arthus,[3] of France, and Uhlenhuth,[4] of Germany, published the results of their experimental work on the injection of proteins in the eyes of animals and the allergic reactions produced. In 1908 Nicolle and Abt[5] demonstrated the possibility of allergic reactions occurring in the eye. The latter observed that when animals were sensitized by an intraperitoneal injection of serum, subsequent intraocular injection of the serum brought about a violent local inflammation. One year later, Sattler[6] observed a slight reaction from a preliminary injection into the eye, but a peculiarly violent reaction followed reinjection at a later date. Subsequently, the works of Wessely,[7] Krusius,[8] Kümmel,[9] Dold and Rados,[10] von Szily,[11] Fuchs and Meller,[12] D. and B. C. Seegal[13] and others have proved that the tissues of the eye can readily be sensitized both locally or as part of a general sensitization; that they are capable of virulent allergic responses; that a flare-up may follow entry of the antigen via the gastrointestinal tract, and that desensitization can be achieved by repeated intravenous injections of the antigen.

FACTORS INFLUENCING THE INCIDENCE OF ALLERGIC PHENOMENA

Hereditary Sensitization.—This is the most important factor in allergic responses and may be considered the exciting cause. It is found in the history of from 50 to 70 per cent of susceptible persons. Only the tendency to hypersensitiveness is inherited, not the allergy itself. The tendency may be transmitted in two ways: (*a*) through the germ plasm of the parents, following the laws of mendelian inheritance, and (*b*) through direct placental permeability. In the latter case, when the sensitizing agent affecting the mother acts directly on the cells of the fetus, active sensitization results; when the antibodies produced by the mother in response to the sensitizing agent are transmitted to the fetus, passive sensitization results. Statistics indicate that the majoriy of allergic persons have one or more antecedents with some type of allergic manifestation and that symptoms will develop in

3. Arthus, N. M.: Compt. rend. Soc. de biol. **4**:817, 1903.

4. Uhlenhuth, P., in Festschrift zum sechzigsten Geburtstage von Robert Koch, Jena, 1903, p. 49.

5. Nicolle and Abt: Ann. Inst. Pasteur **22**:132, 1908.

6. Sattler, C. H.: Arch. f. Augenh. **64**:390, 1909.

7. Wessely, K.: Arch. f. Augenh. **93**:184, 1923.

8. Krusius, F. F.: Arch. f. Augenh. **67**:6, 1910.

9. Kümmel, R.: Arch. Ophth. **77**:393, 1910; **79**:528, 1911.

10. Dold, H., and Rados, A.: Deutsche med. Wchnschr. **39**:1492 and 2254, 1913.

11. von Szily, A.: Die Anaphylaxie in der Augenheilkunde, Stuttgart, Ferdinand Enke, 1914.

12. Fuchs, A., and Meller, J.: Arch. f. Ophth. **87**:280, 1914.

13. Seegal, D., and Seegal, B. C.: Proc. Soc. Exper. Biol. & Med. **27**:390, 1930.

a certain proportion of their offspring. Other of these offspring, while themselves free from manifestations of sensitivity, may again transmit the tendency to their offspring.

The greater or more complete the hereditary influences, (*a*) the earlier the age at which symptoms are apt to appear, (*b*) the more frequent the cutaneous reactions as to positivity and multisensitivity, (*c*) the greater the number of manifestations, (*d*) the greater the number of progeny affected and (*e*) the more likely are the progeny to show the same allergic manifestations as the parents. The time of life this is inherited may be anywhere from a few days to forty or more years. The duration is often lifelong; only a state of "reduced sensitivity" can be attained, and this may not be permanent.

The exact nature of this tendency is not clear. In many instances it is merely evidence of a disturbed endocrine balance with a resulting disturbance of the metabolic and biochemical function. LaGrange[14] considered that a constitutional instability of the equilibrium of the organic colloids may constitute the basis. At any rate, an allergic diathesis must exist in the patient; only then can an atopic substance cause altered reactivity in the tissues.

Acquired Sensitization.—(*a*) Natural (a common manifestation): The allergic response may be brought about by inhalation, ingestion or injection of the atopic substance or by direct contact with it.

(*b*) Induced (a less common manifestation): The allergic response may follow transfusion of sensitized human serum and serum disease.

Nervous or Psychic Disturbances.—These disturbances have been considered by psychologists as capable of provoking allergic reactions, particularly in middle-aged women. However, in view of positive Prausnitz-Küstner reactions obtained with serum from such patients, one can hardly explain satisfactorily the allergic response on a purely psychopathic basis. It is more likely that such patients are primarily allergic, and the psychic trauma pulls the switch.

Nasal Abnormalities.—These abnormalities may indirectly be responsible for an allergic reaction. Infected sinuses provide the bacterial antigen. There may be sensitive areas of tissue responsible for reflex pressure symptoms. Berens[15] mentioned two interesting examples illustrative of the influence of nasal abnormalities. Both patients had atropine blepharoconjunctivitis and were also sensitive to other cycloplegics. When their ethmoid sinuses were cleared surgically, both became desensitized. One of these patients was also hypersensitive to tuberculin and to uveal pigment, but his severe iridocyclitis did not

14. LaGrange, H.: Brit. J. Ophth. **19:**241, 1935.

15. Berens, C., in discussion on Bedell, A. J.: New York State J. Med. **36:** 959, 1936.

improve with injections of tuberculin, uveal pigment or autogenous vaccine, yet the eye quieted promptly when his ethmoid sinuses were drained. Haiman[16] reported 3 cases of vasomotor rhinitis with marked ocular symptoms—pains within and behind the eyes. After treatment of the nose and sinuses, the symptoms disappeared.

Endocrine Disturbances.—Such disturbances appear in the picture in certain cases, although the average allergic patient does not present any definite signs or symptoms of hyperfunction or hypofunction of the endocrine glands. A number of cases have been reported which point to both hyperfunction and hypofunction of the thyroid gland as a factor in some allergic phenomena. The association of allergic conditions with hyperfunction and hypofunction of the gonads has also been observed. Some allergic ocular conditions often cease at puberty when complete readjustment of the endocrine glands occurs, while others begin at the menopause. LaGrange[17] reported an interesting case of a woman in whom vernal conjunctivitis developed after removal of her ovaries at the age of 30 years; the administration of thyroid and ovarian substance cleared up the pathologic condition.

Experimentally, it has been demonstrated that adrenalectomized rats are more susceptible to anaphylactic reactions while normally they are most resistant to the induction of a hypersensitive state. It is also noted that during an acute allergic attack many persons show definite signs of hypofunction of the adrenals, i. e., exhaustion, low blood pressure, hypoglycemia and a dextrose tolerance similar to that found in Addison's disease. Then again, bearing in mind that an injection of epinephrine often relieves the allergic reaction, the possibility of intermittent hypofunction of the adrenals must not be ignored.

FOCAL INFECTION AND ALLERGY

The theory of focal infection is still respected on the basis of simple bacterial metastasis. But many ocular inflammations, supposedly due to bacterial metastasis from remote primary foci, may actually be specific allergic reactions. While clinical proof is inadequate, recent experimental works point to the conclusion that bacterial infection can produce definite hypersensitivity of the ocular tissues. This is accomplished when bacterial products or toxins reach the eye from a remote focus through the blood or lymph. Subsequent absorption of the bacterial products or toxins from the primary focus evokes in this sensitized tissue an allergic inflammatory reaction. This offers some explanation for those ocular conditions known to be due to focal infection, yet isolation of the organism from the secondary focus is not possible.

16. Haiman, J. A.: M. Rec. **147**:101, 1938.
17. LaGrange, H.: Presse méd. **31**:380, 1923.

Shwartzman [18] in 1928 reported a phenomenon of local cutaneous reactivity to Bacillus typhosus filtrate. He found that when a potent bacterial filtrate was injected into the skin of a rabbit, no appreciable reaction resulted other than a rapidly disappearing erythema, perhaps. But if twenty-four hours later the rabbit received the same or another potent filtrate intravenously, there appeared after four or five hours an extremely severe hemorrhagic necrosis at the site of the local injection.

Cassuto,[19] Mossa,[20] Rossi,[21] Fabiani and Gauthier,[22] Mikaelyan and Aronov [23] and, more recently, Sanders [24] studied the ocular possibilities of the Shwartzman phenomenon. The results were indeterminate. However, the mechanism and lesions of this phenomenon suggest that it may be one of the means by which a focus of infection can cause activity in a distant lesion. By absorption of bacterial toxin from a distant focus of infection, the continued activity of an ocular lesion, if not the primary inflammation, might be explained by the Shwartzman phenomenon. It may also serve to explain the mechanism in the production of the lesions in Eales' disease.

THE ALLERGIC PERSON

It is generally conceded that 10 per cent of the population are allergic to one thing or another. Positive reactions of the skin or mucous membranes to specific allergens are obtainable in over 50 per cent of cases. The allergic person has less disease than others and a greater degree of intelligence. He is more emotional and temperamental and has, in general, a more alert nervous system. One may suspect an allergy in the presence of the following features:

1. A personal history which reveals evidence of previous allergic phenomena: food dislikes and disagreements, childhood eczema, nettlerash, dermatitis, urticaria, asthma, vasomotor rhinitis and recurrent bronchitis.

2. A history of allergy in the parents, grandparents, brothers and sisters, offspring, uncles or aunts.

3. Periodic recurrence of symptoms, not relieved by therapy (excluding adrenalin), in the absence of any definite pathologic process.

4. Chronicity of a condition or the rapid healing of lesions, only to be followed by the development of new ones in succession.

18. Shwartzman, G.: J. Exper. Med. 48:247, 1928.
19. Cassuto, N.: Sperimentale, Arch. di biol. 87:191, 1933.
20. Mossa, G.: Boll. d'ocul. 14:1031, 1935.
21. Rossi, G.: Boll. d. Soc. med.-chir. di Modena 35:193, 1935.
22. Fabiani, G., and Gauthier, A.: Compt. rend. Soc. de biol. 124:51, 1937.
23. Mikaelyan, R. K., and Aronov, D. M.: Vestnik oftal. 11:55, 1937.
24. Sanders, T. E.: Am. J. Ophth. 22:1071, 1939.

5. Eosinophilia not explained by other pathologic involvement; eosinophilia in the local secretion. This should not be regarded as a fundamental reaction in allergy but rather as a clinical finding which is a useful guide in such conditions.

6. Favorable response to a solution of epinephrine hydrochloride, by injection or locally.

7. Signs and symptoms which may be explained by an increased permeability of the capillaries or spasm of smooth muscles.

8. Biochemical analysis which shows a tendency to a low blood sugar, a low cell chloride content, a high amino-acid content of the blood, a normal blood cholesterol and calcium with an inclination toward low figures for the blood phosphorus and potassium; also, a well marked hypochlorhydria on fractional analysis of gastric contents and evidence of some hepatic insufficiency.

9. A low blood pressure, brought about by the liberation of histamine, which dilates the arterioles (although Waldbott[25] described cases of arterial hypertension due to allergic causes).

10. Clinical evidence of endocrine imbalances, involving the adrenals, thyroid or gonads, particularly if associated with any of the foregoing symptoms.

EVALUATION OF CUTANEOUS REACTIONS

The evaluation of the results of cutaneous reactions is best summed up by Bray,[26] who stated that a positive cutaneous reaction may be interpreted as indicating:

(*a*) The specific cause of the disease—a reaction of great utility for eliminative or desensitization measures.

(*b*) A definite sensitivity but not necessarily the cause of the condition in question—a reaction of value from the prophylactic standpoint.

(*c*) A latent sensitivity that has not yet matured, which may be due to an absence or insufficient contact with the allergen.

(*d*) A specific sensitivity in a person who has lost or never developed sensitivity clinically. Positive cutaneous reactions may still be elicited even after successful desensitization measures have been carried out.

Temporary pseudospecific or nonspecific reactions as well as traumatic reactions must be excluded.

A negative cutaneous reaction may be interpreted as indicating:

(*a*) A true absence of sensitivity.

25. Waldbott, G. L.: Hypertension Associated with Allergy, J. A. M. A. **94:** 1390 (May 3) 1930.

26. Bray, G. W.: Recent Advances in Allergy, Philadelphia, P. Blakiston's Son & Co., 1931, pp. 68-69.

(*b*) A very early state in the development of sensitivity, where sufficient sensitivity has not yet been acquired to react with the allergen when applied locally.

(*c*) Unreliability of the extracts employed.

(*d*) A false result occurring in a patient who clinically demonstrates sensitivity to the particular factor. Most drugs give negative reactions; frequently pollens give negative reactions in young children and quite often foods give such reactions in infants and adults, while in general bacteria and molds give doubtful reactions.

ALLERGIC MANIFESTATIONS OF INTEREST TO THE OPHTHALMOLOGIST

LIDS

The skin of the lids and that immediately surrounding them reacts in a manner similar to that of the skin elsewhere. The more common allergic phenomena observed in hypersensitive persons are: urticaria with itching and redness from the use of yellow mercuric oxide; angioneurotic edema and dermatitis with intense itching, redness and edema, following exposure to extremes of temperature, ingestion of certain foods and of drugs such as quinine and coal tar products, extension from the nose in hay fever and contact with face powders or eye cosmetics; intense circumscribed redness of the skin resembling erysipelas, following the use of a 1 per cent solution of atropine or a 2 per cent solution of homatropine; chronic blepharitis, resistant to all forms of local treatment, found in association with eczema; and poison ivy or poison oak dermatitis from contact.

Ruedemann [27] reported the occurrence of a stye in a boy forty-eight hours after eating chocolate. Hughes [28] mentioned a case of recurrent styes which resisted all forms of treatment—refraction, autogenous vaccine and cod liver oil—but disappeared when the patient eliminated peanuts from her diet. Only after she ate peanuts would styes return in a few days.

CONJUNCTIVA

The sensitized conjunctiva reacts to contact with a specific allergen with a boggy infiltration. When the patient is withdrawn from contact with the atopic substance, this rapidly subsides. In cases of chronic involvement, especially with secondary infection, a round cell infiltration complicates the picture. Eosinophils may be found in the secretion.

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27. Ruedemann, A. D.: Ohio State M. J. **30**:304, 1934.

28. Hughes, W. F., in discussion on Larkin, B. J.: J. Indiana M. A. **28**:267, 1935.

Investigation by Schlecht [29] has shown the eosinophilia is closely related to, or dependent on, protein absorption.

There is ample evidence that conjunctivitis in hypersensitive persons, on exposure to the specific allergen, is a definite clinical entity. The atopic substances responsible for most simple conjunctivitis comprise foods (onion, tomato and egg), pollens, cereals, animal dust, feathers, house dust, corn dust, orris powder, cat hair, drugs (physostigmine salicylate, butyn, atropine, ethylmorphine hydrochloride and ethylhydrocupreine hydrochloride), cosmetic dyes, various serums, bacterial proteins and fungi. In the case of drugs, sensitization need not be to the entire drug but may be to certain radicles thereof. Conjunctival hypersensitivity is a common observation among patients ailing with asthma, hay fever and vasomotor rhinitis. When chemicals are suspected as being the causative allergen, however, one must differentiate simple, chemical irritation from true allergic manifestation.

Depending on the causative factor, allergic conjunctivitis may appear clinically in three forms: (*a*) the acute edematous type; (*b*) the eczematous type, and (*c*) the chronic, recurrent, irritative type. The acute edematous type is characterized by sudden onset, edema, conjunctival congestion and lacrimation. It is most commonly seen associated with asthma and hay fever. The so-called edematous eczematous type is characterized by eczema of the lids and neighboring skin, edema of the lids, profuse lacrimation, conjunctival congestion and slight chemosis. It is observed after the use of drugs, such as butyn and atropine, and always accompanied by marked hypersensitivity of the skin, as shown by positive patch tests with the offending substances. The chronic, recurrent, irritative type is often associated with low grade folliculosis with sharp exacerbations and normal bacteriologic findings. It is most often caused by pollens and epidermal allergens, and the conjunctivitis may be the only manifestation of allergy in the patient.

I have observed the sudden development of marked chemosis of both bulbar conjunctivas in a boy of 8 after he handled some plant life while at a summer resort. The edema was so intense that only partial closing of the lids was possible. Instillation of epinephrine hydrochloride proved effective, quickly. Vaughan [30] mentioned a case in which an urticarial wheal appears on the bulbar conjunctivas as an acute reaction after the patient eats cucumbers and sometimes after he eats wheat. The lesion always occurs in the left eye and is rarely accompanied by any other cutaneous or visible response of the mucous membrane. It clears up rapidly after the instillation of epinephrine hydrochloride.

Vernal Conjunctivitis.—A number of theories have been advanced concerning the causation of vernal catarrh, but three stand out promi-

29. Schlecht, H.: Arch. f. exper. Path. u. Pharmakol. **67**:137, 1912.

30. Vaughan, W. T.: Practice of Allergy, St. Louis, C. V. Mosby Company, 1939, p. 151.

nently: 1. It may be a constitutional expression of an endocrinopathy.
2. It may be related to a vagotonia coupled with adrenal deficiency.
3. It may be an allergic reaction of the conjunctiva due to hypersentitivity and intoxication from specific allergen.

Experimentally, the results of more recent studies have answered a number of questions, so that the allergic nature of vernal catarrh can no longer be disputed. First, it has been demonstrated that a local hypersensitivity to a specific allergen may be produced in the conjunctiva. Second, many patients with vernal conjunctivitis (10 per cent) give a definite history of other allergic conditions. The literature contains numerous reports of the frequent association of vernal conjunctivitis with hay fever, vasomotor rhinitis and asthma. Also, many patients (30 per cent) give a family history of allergy, either definite or questionable. Third, the greater percentage of patients with vernal catarrh are sensitive to one or more atopic substances. Fourth, the pathologic picture of vernal catarrh can be reconciled with the pathologic picture of the known allergic reactions of the mucous membranes and skin; the phlyctenule of the limbic type has been clearly demonstrated to be an allergic reaction of a sensitized conjunctiva to intoxication with the specific allergen, while the connective tissue proliferation and cellular infiltration of the flat follicles have been demonstrated to be a reaction comparable to that occurring in asthma and eczema.

Clinically, an allergic causation is suggested by the seasonal recurrence of the attacks, the itching, the type of secretion with the presence of eosinophils, the comparative absence of bacteria, the course of the disease and the tendency to attack the young. Lehrfeld,[31] in studying 87 cases at the Wills Hospital in Philadelphia, found the distribution in the age groups to be as follows: 39 per cent in the group under 10 years of age; 22 per cent in the group from 11 to 20 years of age; 12 per cent in the group from 21 to 30 years of age; 6 per cent in the group from 31 to 40 years of age and the remaining 21 per cent in the group over 40 years of age.

Trachoma.—Knowledge of the immune reaction in trachoma and of the bacterial causation of the disease is still in a state of confusion. In 1928 Noguchi [32] advanced the theory that Bacterium granulosis was the offender in trachoma. Subsequently, his conclusions were upset by investigators who failed to isolate the organism from many of their patients with trachoma. Noguchi's work stimulated investigation of the question of specific immune reactions in trachomatous patients to B. granulosis. Thus far, however, there has been no proof to show any specific hypersensitivity or immune reactions to the disease.

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31. Lehrfeld, L.: Vernal Conjunctivitis: Observations on Eighty-Seven Cases at the Wills Hospital (1929-1931), Arch. Ophth. **8**:380 (Sept.) 1932.

32. Noguchi, H.: J. Exper. Med. **48** (supp. 2):1, 1928.

Pascheff [33] studied the relation of trachoma to tuberculosis from the allergic standpoint. He concluded that trachoma is an endogenous, constitutional, lymphadenomatous disease of the conjunctiva and not an inflammatory lymphatic infiltration in which the follicles are accidental manifestations. He further ventured the suggestion that trachoma may be an anaphylactic symptom of latent tracheobronchial tuberculosis, a view shared by Tschirkovsky. [34]

Lemoine [35] reported 4 cases of trachoma with recurrence each summer and hypersensitivity to pollens. A number of cases of a condition resembling trachoma have been observed in farmers during the spring plowing season and treated as such, whereas, actually, the pathologic process was brought about by hypersensitiveness to weeds and other plants.

Fungus Conjunctivitis.—In certain localities a great many persons are allergic to fungi. Durham [36] has pointed out that the atmospheric concentration of fungus spores may approximate that of ragweed pollen grains. Hypersensitivity may be developed when fungi come in contact with mucous membranes, by the absorption of allergen material; subsequent contact with the same fungi brings on the allergic reaction.

While most persons with fungus hypersensitivity show respiratory symptoms—allergic rhinitis and asthma—Simon's [37] patient showed symptoms solely of conjunctivitis, i. e., recurrent attacks of conjunctival redness, itching and burning in the eyes for four years. The symptoms were most pronounced during June, July and August and disappeared after thirty-one desensitization injections of Alternaria and Cladosporium, both of which gave definitely positive cutaneous reactions by the scratch method.

Phlyctenular Conjunctivitis.—This type of conjunctivitis will be considered subsequently with phlyctenular keratitis.

CORNEA

Although the cornea is an avascular tissue, it appears from the experimental results available that it does not differ from other body tissues in the reaction to the parenteral introduction of foreign protein. In such a case there is definite formation of antibodies with absorption of foreign protein from the cornea and the formation of immune reactions in the entire organism.

33. Pascheff, C.: Am. J. Ophth. **15**:690, 1932.
34. Tschirkovsky, V., abstracted, Am. J. Ophth. **11**:329, 1928.
35. Lemoine, A. N.: Tr. Am. Acad. Ophth., 1925, p. 198.
36. Durham, O. C.: J. Allergy **8**:480, 1937.
37. Simon, F. A.: Allergic Conjunctivitis Due to Fungi, J. A. M. A. **110**:440 (Feb. 5) 1938.

Corneal Ulcers.—A number of reports of cases of corneal ulcers associated with hypersensitivity appear in the literature. Wiener [38] observed a case in which ocular involvement from the use of Lash-Lure progressed to blindness. One cornea was practically destroyed and the other rendered opaque with a complicating cataract. Zerfoss [39] described a case in which eyelash dye was the offender. This patient's scratch test to the dye (paraphenylenediamine) was 4 plus. In another case ulcerative keratitis developed which was confined to the upper temporal quadrant and was associated with gastrointestinal allergic symptoms, dermatitis and headaches. Allergic tests were positive for a number of substances, and other etiologic factors were excluded. Mention is also made of the case of Wilmer and Woods in which ulceration resulted from contact with corn dust. Lemoine [35] reported 2 cases of dendritic ulcers; in 1 the patient was hypersensitive to chocolates and in the other to pollens. He also cited a case of herpes of the cornea due to hypersensitivity to chocolate and corn; withdrawal of these foods caused healing, while return to these foods caused a recurrence of the herpes.

Phlyctenular Keratoconjunctivitis.—The common allergic reaction of the sensitized cornea to tuberculoprotein appears to select the epithelium as its favored site, in the formation of the phlyctenule. The first inkling that the phlyctenule is a tuberculous formation was suggested by Schick, when he noted localized swelling at the corneal margin in the Calmette reaction. It is a rather common clinical observation that the instillation of tuberculin into the conjunctival sac of patients hypersensitive to tuberculin may cause the appearance of phlyctenules. Weekers [40] pointed out that tuberculin instilled into the conjunctival sac of a person who has recovered from phlyctenules will produce a second attack. In fact, since von Szily [41] in 1917 advanced the theory that the phlyctenule, which he, too, considered tuberculosis, is an allergic reaction, much evidence has piled up in favor of it. It is now held conclusive that the phlyctenule represents an allergic reaction of the sensitized epithelial surface of the cornea and conjunctiva. Sensitization may result either from a small, early, tuberculous focus in the eye or as a part of the general hypersensitiveness to tuberculoprotein from some more remote focus. Intoxication may result either from the direct introduction of tuberculous material into the eye or from tears or the blood stream, following any alteration of the general tuberculous status which liberates tuberculoprotein.

It is possible that sensitization and intoxication with protein material other than tuberculin may be the cause of phlyctenules. Experimentally, these have been produced in animals by sensitization and intoxication

38. Wiener, M.: South. M. J. **28**:1011, 1935.
39. Zerfoss, K. S.: J. Tennessee State M. A. **28**:93, 1915.
40. Weekers, L.: Arch. d'opht. **44**:411, 1927.
41. von Szily, A.: Clin. opht. **21**:251, 1917.

with antigens other than tuberculin. Lemoine [42] reported 2 cases of phlyctenular keratitis, one apparently due to hypersensitivity to strawberries and the other to face powder. Schieck [43] reported a case in which a patient with gonorrheal arthritis contracted accidental gonorrheal conjunctivitis which was characterized by the appearance of definite phlyctenules. It is the high incidence of tuberculin hypersensitivity in phlyctenulosis which indicates that products of the tubercle bacillus are the common materials responsible.

The allergic phenomenon also provides a common basis for the claims of dissenters with regard to the nature of the disease. It is the opinion of some that phlyctenular disease is secondary to sinus disease, especially of the ethmoid sinuses. Here it may be assumed that the eye has become sensitized either to the specific exciting agent or to the metabolic products from the infected focus; further absorption of such material produces an allergic reaction in the eye manifested as phlyctenules. Others hold the phlyctenule to be associated with irritability of the vagus nerve, the result of faulty carbohydrate metabolism. Recent studies on the hapten action of carbohydrates may explain this observation, too, along similar lines.

Interstitial Keratitis.—Tuberculous Interstitial Keratitis: Although the case in favor of an allergic factor in tuberculous interstitial keratitis is not as potent as that of the phlyctenule, experimental studies indicate it is probable that allergy may influence the type and progress of such a lesion. There is evidence which may be interpreted to support the contention that toxic or allergic tuberculous interstitial keratitis is possible. Igersheimer [44] gave normal rabbits an intracorneal injection of a weak suspension of bovine tubercle bacilli. Opacities resulted, but soon disappeared. A few days later there appeared conjunctival hyperemia and a corneal opacity at the site of injection, surrounded by diffuse interstitial infiltration, with a tendency to ulcerate. Subsequent microcopic examination of these eyes revealed the fact that bacilli were found only at the site of injection but not in the infiltrated cornea. Evidently, toxins and not bacilli brought about the infiltration. When tuberculous rabbits were given similar injections, a violent inflammatory reaction set in, comparable to the reaction occurring in other tuberculous tissue on the reinjection of tubercle bacilli. The latter type of reaction presents all the earmarks of an allergic, necrotizing one.

Samoilov [45] noted that animals with experimental tuberculous keratitis showed focal reaction in the cornea after subcutaneous injections of tuberculin. Thereupon, he administered rather large injections of

42. Lemoine, A. N.: Ocular Anaphylaxis, Arch. Ophth. **1**:706 (June) 1929.
43. Schieck, F.: München. med. Wchnschr. **79**:6, 1932.
44. Igersheimer, J.: Klin. Monatsbl. f. Augenh. **69**:226 and 486, 1922.
45. Samoilov, A. J.: Klin. Monatsbl. f. Augenh. **87**:215, 1931.

tuberculin subconjunctivally to 16 patients with tuberculous keratitis. All showed definite focal reactions in the eyes, which he believed not only confirmed the diagnosis of the tuberculous nature of the ocular condition but gave information as to the general immune-biologic condition of the entire organism.

Verhoeff [46] and Finnoff [47] demonstrated a sclerokeratitis comparable to that observed in human beings with injections of dead tubercle bacilli into the vitreous and anterior chamber. Such reactions are regarded either as a direct toxic action of the tuberculoprotein on the ocular tissues or as the result of sensitization and intoxication from the tuberculoprotein. The delay in the development of keratitis after the injection of dead tubercle bacilli which Finnoff also observed may be interpreted as a definite allergic manifestation.

Syphilitic Interstitial Keratitis: Experimental analogy indicates that certain cases of syphilitic interstitial keratitis may be definitely allergic. In 1911 Wessely [48] suggested that syphilitic interstitial keratitis might be related to anaphylaxis. Animal experimentation led him to the conclusion that the condition was due to a specific corneal hypersensitivity and intoxication. Igersheimer [49] pointed out that in hereditary syphilis the cornea contains spirochetes which sensitize it to the condition. Should spirochetes come to life subsequently in another part of the body and liberate their toxins in the blood, an anaphylactic reaction in the hypertensive cornea results, i. e., interstitial keratitis. Others have been unable to demonstrate spirochetes in the cornea in this condition.

Clinically, there are certain observations which suggest that the keratitis in some cases may be allergic. The sudden occurrence of interstitial keratitis in a patient under active treatment for syphilis with preparations of the heavy metals while the infection is elsewhere following a favorable course has often been noted; also, the stubbornness of the condition to treatment with arsenicals. If actual invasion of the cornea by spirochetes took place in all instances of this condition, one would expect definite improvement in the eye to follow arsenical treatment, since it is known that arsphenamine injected intravenously rapidly reaches the cornea. Hence, an inference is drawn that in certain cases recurrent interstitial keratitis in persons with congenital syphilis is probably an allergic phenomenon, a sensitization of the cornea being produced through invasion by spirochetes either in fetal life or early in the course of the disease. Subsequently, the syphilitic status being altered somewhat by the arsenical treatment, large amounts of disin-

46. Verhoeff, F. H.: Tr. Am. Ophth. Soc. **13**:469, 1913

47. Finnoff, W. C.: Am. J. Ophth. **7**:365, 1924.

48. Wessely, K.: München. med. Wchnschr. **58**:1713, 1911.

49. Igersheimer, J.: Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **39**:251, 1913.

tegrating syphilitic virus are liberated. This, when carried to the eye via the blood or lymph, produces an intoxication of the sensitized cornea, clinically manifested as interstitial keratitis.

SCLERA AND EPISCLERA

Both scleritis and episcleritis have in some instances been attributed to allergy, but definite proof is lacking. However, since focal infection may be an etiologic factor, these conditions may be considered allergic on the basis that bacterial infection is capable of producing hypersensitivity of ocular tissues, as explained previously.

UVEA

Iritis and Iridocyclitis.—There is considerable evidence to show that allergic sensitization is a factor in the causation of inflammations of the uveal tract. In fact, some cases of recurrent iritis and uveitis can be explained only on an allergic basis. Kolmer [50] expressed the belief that all types of endogenous iritis are due to (1) the presence of microorganisms in the iris (direct), (2) the action of bacterial toxins in the iris (indirect) or (3) acquired allergic sensitization of the ocular tissue to bacterial products occurring in remote foci of infection. In most cases of chronic recurrent iritis and iridocyclitis, the tissues of the iris acquiring allergic sensitization to streptococci and their toxins, the lesions are due to allergic shock reactions. This theory is strengthened in many cases of active iritis by the favorable response when the disease is treated with streptococcic bacterial antigen.

Allergic response in the uvea may occur not only from bacteria and their toxic products but from other foreign proteins, existing in minute quantities insufficient to produce systemic symptoms. Experimentally, iritis has been produced by first immunizing animals by subcutaneous, intravenous or intraperitoneal injections of a foreign protein, then injecting the same substance after an interval. The length of time after inoculation before appearance of the lesions, sufficient time for sensitization and intoxication to occur, and the caseating nature of the lesions point to an allergic basis.

With regard to the influence of allergy on uveal tuberculosis, there is much experimental work. That of LaGrange,[51] Stock,[52] Rollet and Aurand,[53] Friedenwald,[54] Montalti,[55] Samoilov,[56] Finnoff [47] and others

50. Kolmer, J. A.: Am. J. Ophth. **14**:217, 1931.
51. LaGrange, H.: Bull. et mém. Soc. franç. d'opht. **16**:88, 1898.
52. Stock, W.: Arch. f. Ophth. **66**:1, 1907.
53. Rollet, E., and Aurand: Rev. gén. d'opht. **21**:1, 1907.
54. Friedenwald, J. S.; Rothschild, H., and Bernstein, C.: Bull. Johns Hopkins Hosp. **54**:232, 1934.
55. Montalti, M.: Ann. di ottal. e clin. ocul. **55**:555, 1927.
56. Samoilov, A. J.: Arkh. oftal. **7**:721, 1930.

and the 2 case records reported by Verhoeff [57] make it appear clearly that allergy and immunity influence the lesions of ocular tuberculosis both in animals and in man. When tubercle bacilli reach the eye of a normal animal, a slowly progressing tuberculous lesion characterized by tubercle formation is produced. When tubercle bacilli reach the eye of a tuberculous subject, there is produced an acute, caseating lesion with sharp inflammatory reaction. The spreading, caseating type of lesion is probably produced by large numbers of tubercle bacilli in an allergic subject with low resistance. The sharp, acute, rapidly localized lesion is probably produced by a small number of tubercle bacilli in a subject with a high degree of allergy and resistance. Miliary lesions have a tendency to coalesce and caseate when allergy is great.

The small whitish-gray "Koeppe nodules" described by Koeppe [58] in connection with tuberculous iritis and usually found at the pupillary margin of the iris bear a possible relation to allergy. Although described in sympathetic ophthalmia, leprosy and tropical syphilis, these nodules are usually seen in low grade uveitis and are believed to be indicative of a tuberculous process or a high degree of tuberculous hypersensitivity. In spite of the absence of experimental evidence to sustain the view, the striking histologic similarity of these nodules to phlyctenules strongly suggests they may be a manifestation of allergic intoxication in sensitized iris tissue.

Clinically, bacterial allergy is to be thought of when the cardinal symptoms of iritis develop rapidly and are soon followed by red and edematous eyelids, intense congestion of the bulbar conjunctiva, hazy cornea and hypopyon, with consequent serious impairment of vision. The allergic nature is further emphasized when the eye makes a speedy recovery within forty-eight hours or so and when such an attack occurs in association with some other bacterial infection elsewhere in the body.

Sympathetic Ophthalmia.—Elschnig [59] in 1910 introduced the theory that uveal pigment acts as an allergen in the causation of sympathetic ophthalmia. He demonstrated that uveal pigment has antigenic properties, as shown by the complement fixation. His theory assumed the absorption and general dissemination of uveal pigment following penetrating injury to the eye, with the production of hypersensitivity of the organism as a whole and especially of the fellow eye. As this uveal pigment continued to be absorbed from the exciting eye, allergic intoxication of the sensitized tissue resulted and made it possible for some unknown factor to produce the clinical picture of sympathetic ophthalmia.

57. Verhoeff, F. H.: Histologic Observations in Case of Localized Tuberculous Chorioretinitis, Arch. Ophth. **1**:63 (Jan.) 1929.

58. Koeppe, L.: Arch. f. Ophth. **92**:115, 1917.

59. Elschnig, A.: Arch. f. Ophth. **76**:509, 1910.

Woods[60] and others subsequently confirmed Elschnig's work. It explained the lapse of time (two to six weeks) between an injury to the exciting eye and the development of sympathetic ophthalmia in the sympathizing eye; it also explained why no bacteria could be found as the agents responsible for sympathetic ophthalmia and brought to light the fact that hypersensitivity to uveal pigment resulted only after penetrating wounds of the eye.

The available evidence indicates that the development of allergy to uveal pigment is the essential predisposing factor necessary to permit the outbreak of sympathetic ophthalmia and that some other unknown factor acts as the actual spark which initiates the process. It is probable that the development of allergy to uveal pigment alters the normal immune-biologic defense mechanism of the eyes and so allows other noxious agents to produce the picture. Once initiated, pigment allergy is again the factor which determines the characteristic histologic picture.

After studying the histologic picture of sympathetic ophthalmia, Friedenwald[61] concluded that the characteristic microscopic changes are compatible with the allergic theory of this condition. He noted the following features:

1. Phagocytosis of melanin granules by epithelioid cells and giant cells formed a prominent feature of the lesions of sympathetic ophthalmia in the uveal tract, in the episcleral tissues and in the retina and was absent or insignificant in other intraocular inflammatory diseases.

2. The reaction in cases of sympathetic ophthalmia to the intradermal injections of uveal pigment suspension had all the characteristics of the inflammatory reaction in the eye.

3. The cutaneous reaction of normal controls and of patients with nonsympathetic uveitis generally differed from that of patients with sympathetic ophthalmia.

False positive reactions, however, were encountered, which made it necessary to conclude that if allergy to uveal pigment is responsible for the characteristic lesions of sympathetic ophthalmia, some other factor was required to release the uveal pigment from the melanophores and make it available for the allergic reaction. A study of the Dalen-Fuchs nodules, which are characteristic of sympathetic ophthalmia, leads to the hypothesis that the additional factor required for the initiation of the inflammatory reaction is a proliferation of intraocular melanophores.

Endophthalmitis: A number of cases of endophthalmitis have been reported in which the clinical picture is one of a protracted low grade iridocyclitis, either traumatic or postoperative. This condition develops

60. Woods, A. C.: Arch. Ophth. 46:283, 1917.
61. Friedenwald, J. S.: Am. J. Ophth. 17:1008, 1934.

synchronously with allergy to uveal pigment. The patients show positive reactions to intracutaneous pigment tests, and while enucleation may be indicated clinically, sympathetic ophthalmia does not follow.

The condition in these cases is similar to endophthalmitis phacoanaphylactica described by Verhoeff and Lemoine [62] in 1922 and constitutes a definite clinical entity. The endophthalmitis may be dependent on the development of allergy to uveal pigment, or the development of pigment allergy may so impair the immune-biologic defense mechanism of the eye that normal healing is seriously impaired.

<div align="center">LENS</div>

In spite of the abundance of experimental work done since Uhlenhuth [63] initiated the study of the antigenic properties of the crystalline lens protein, only two conclusions are definitely established—its organ specificity and its lack of species specificity.

Endophthalmitis Phacoanaphylactica.—The ophthalmic surgeon is quite familiar with the severe intraocular inflammatory reaction observed when lens cortex is liberated in the anterior chamber either in trauma or following surgical extraction of a cataract. Patients so affected usually give a positive reaction to lens protein in advance. The inflammation varies with the amount of cortical matter present and the degree of hypersensitivity of the patient. Cataractous lens protein in the anterior chamber is more toxic than normal lens substance. The evidence so far available indicates that postoperative reaction following absorption of lens cortex may be considered a definite allergic phenomenon and the condition of endophthalmitis phacoanaphylactica, a concrete clinical entity.

Goodman [64] has made a study of hypersensitivity to lens protein. Of 700 patients tested intracutaneously with bovine lens antigen, approximately 5 per cent showed reactions to 2 plus or greater. These were regarded to be truly hypersensitive to lens protein. He expressed the belief that this was acquired not congenital, and that the cataractous cortical material was the chief antigenic factor.

Cataract.—In 1868 Rothmund [63] reported the occurrence of cataracts in connection with cutaneous changes. Since then, reports of cataracts in young allergic persons have appeared in the literature from time to time. Andogsky [63] applied the term "cataracta dermatogenes" to

62. Verhoeff, F. H., and Lemoine, A. N.: Endophthalmitis Phacoanaphylactica, in An International Congress of Ophthalmology, Washington, 1922, Philadelphia, William F. File Company, 1922.

63. Cited by Ollendorff, H., and Levy, G.: Arch. f. Dermat. u. Syph. **164**:683, 1932.

64. Goodman, E. L.: Endophthalmitis Phaco-Anaphylactica: Clinical Study, Arch. Ophth. **14**:90 (July) 1935.

bilateral cataracts associated with a cutaneous eruption in a youth. Kurz [63] reported the occurrence of bilateral lenticular opacities associated with eczema in a person aged 21. Davis [63] reported a similar combination in a girl of 15. Lowenstein,[63] Gault [65] and others have observed cases of bilateral cataract associated with neurodermatitis. Daniel [66] reported opacification of the lens accompanied by cutaneous manifestations in 3 young adults: (1) a girl of 17 with rapidly developing cataracts and a definite allergic history, both personal and familial; (2) a girl of 17 with the same history but lenticular changes at the time of examination only in the right eye and (3) a man of 35 with bilateral cataracts and a personal history of allergy.

I have recently observed bilateral cataract associated with neurodermatitis in a man of 29. The cutaneous lesion first appeared three years before the time of my examination. The visual loss, which was more rapid in the right eye than in the left, was first noted eight months before the examination. The cataract in the right eye matured rapidly, and vision in the left eye was reduced to 20/70. There was no history of allergy in his family, i. e., in parents, brothers or sisters. The only allergic manifestation in the patient was attacks of hives, off and on, for one year, about four years before I observed him.

Evidently the lens shares in the changes produced in other tissues of ectodermal origin under the influence of allergens. This is not difficult to imagine when one recalls that the lens is nourished and "purified" by the aqueous—the product of the ectodermal epithelium of the ciliary body. Any changes in these cells, in the composition of the aqueous or in the level of permeability and selectivity of the lens capsule instigated by reaction to allergens may therefore interfere with the normal metabolism of the lens and induce opacification.

The cataracts occurring in allergic persons have certain characteristics. These may be summed up as follows: They begin in young adult life; they are always bilateral and they occur in eyes which were previously entirely normal.

OPTIC NERVE AND RETINA

In some cases of retrobulbar neuritis, damage to the optic nerve may be attributed to an increased tissue sensitivity to tobacco, alcohol, quinine and arsenicals. In other cases, protein or bacterial allergy may precipitate the unfavorable tissue response.

Retinal allergy manifests itself chiefly in the effects of increased permeability of the capillaries and its consequences.

Retinal Hemorrhages.—The characteristic allergic retinal hemorrhages are those (superficial or deep) which vary rapidly in appearance

65. Gault, N.: Bull. Soc. d'opht. de Paris, March 1933, p. 280.
66. Daniel, R. K.: Allergy and Cataracts, J. A. M. A. **105**:481 (Aug. 17) 1935.

and location. It is possible that the evanescent, canoe-shaped hemorrhages with white centers observed at times, particularly in subacute bacterial endocarditis and severe anemias, are of this nature. Shwartzman's phenomenon may explain the mechanism of the hemorrhages as well as the recurrent retinal hemorrhages in young adults (Eales' disease).

Aubineau [67] suggested the theory that recurrent intraocular hemorrhages of adolescence are probably the result of anaphylactic changes in hemophilia. Bedell [68] described allergic reactions in the retina in 2 cases. In 1 case the entire retina was edematous and overspread with superficial striate and somewhat deeper surrounding hemorrhages. The veins were distended but not overtortuous and in places were partially hidden by the overlying retina. The lumen of the arteries was irregular. The macula was clearly outlined, irregular, dark and oval and surrounded by deep retinal hemorrhages—a shower of petechial hemorrhages. These all disappeared after about two and one-half months. In the other case the allergic reaction followed the injection of tetanus antitoxin. The nerve head was completely obscured by thick, white, edematous swellings, which appeared like irregular balloons of various sizes and prominence, with several superficial hemorrhages over them. The arteries were normal, but the veins were at least twice their normal size. Plumer [69] reported a case of sudden loss of vision with congestion and haziness of the left macula. Removal of tonsils and infected teeth, withdrawal of chicken meat, peanuts, cottonseed and beans from the diet and removal from exposure to early grass pollens resulted in a cure.

Retinal Detachment.—In the absence of a history of trauma, high myopia, tumor of the choroid or some other common etiologic factor known to influence retinal detachment, one must bear in mind the allergic factor as a possible cause (preceded by edema), particularly when there is a definite history of personal or familial allergy. This view has been expressed by several. Balyeat [70] reported total bilateral amaurosis from progressively detaching retinas in a girl of 17 who gave a history of persistent allergic phenomena which commenced early in life. She had eczema at 3 months of age, asthma and hay fever since 12 months of age and persistent vasomotor rhinitis since infancy. Tests made by intradermal and patch methods revealed sensitivity to silk (intradermal and contact), milk (intradermal) and egg (intradermal).

67. Aubineau: Arch. d'opht. **31**:372, 1920.

68. Bedell, A. J.: Stereoscopic Fundus Photography, J. A. M. A. **105**:1502 (Nov. 9) 1935.

69. Plumer, J. S.: Retinal Allergy: Report of Case, Arch. Ophth. **17**:516 (March) 1937.

70. Balyeat, R. M.: Am. J. Ophth. **20**:580, 1937.

Prewitt[71] reported a case of retinal detachment, probably of allergic origin. The patient was 62 years old and gave a past history of urticaria and angioneurotic edema. On one occasion following the ingestion of turkey liver, marked edema of the jaw and cheeks developed, accompanied by large blebs on the cornea of the left eye. Previous to complete retinal detachment, several attacks of transient blindness occurred, which were usually associated with generalized angioneurotic edema and urticaria. In associating these retinal detachments with the patient's tendency to allergic edema, it is logical to assume that the retina would be subject to reactions similar to those of other structures derived from the same embryologic ectoderm, particularly the skin.

I am of the opinion that retinal detachment observed to come on suddenly during the administration of insulin to diabetic patients may be explained on an allergic basis. A number of cases of insulin allergy have been observed. Williams[72] reported a case of sensitivity to pork insulin. The allergic phenomena—colonic hyperirritability with edema of the eyelids—cleared up on changing to beef insulin. The reaction is found to be more severe when insulin is resumed after a prolonged period of abstinence.

MUSCLES

For the sake of completeness I have included a case of allergy reported by Lemoine,[35] involving the extraocular muscles. The patient experienced attacks of diplopia associated with severe vertigo and scintillating scotoma, not followed by headaches. The attacks were due to cheese. When this was removed from the diet, the attacks disappeared, only to return on ingestion of cheese.

CONCLUSIONS

Present knowledge of experimental and clinical allergic phenomena of the eye makes it necessary for the ophthalmologist to keep in mind "hypersensitivity" as an etiologic factor in many common ocular conditions. Allergy no longer concerns the immunologist alone. The practical applicatiton of this knowledge, however, is restricted to: (1) the therapeutic use of tuberculin in tuberculosis of the eye; (2) the therapeutic use of uveal pigment in sympathetic ophthalmia and (3) desensitization of patients with cataract who are sensitive to lens cortex with lens protein prior to extraction of the cataract.

71. Prewitt, L. H.: Retinal Detachment Due to Allergy: Report of a Case. Arch. Ophth. **18**:73 (July) 1937.

72. Williams, J. R.: Second Case of Gastro-Intestinal Allergy Due to Insulin, J. A. M. A. **100**:658 (March 4) 1933.

News and Notes

EDITED BY W. L. BENEDICT

PERSONAL

Dr. William Burton Clark, of New Orleans, has been appointed head of the department of ophthalmology in the School of Medicine at Tulane University. Dr. Clark has been a member of the professorial staff of the department since 1933. He will assume his new duties September 1, succeeding Dr. W. R. Buffington, who has retired to devote his full time to private practice.

Dr. Le Grand H. Hardy has been appointed assistant clinical professor of ophthalmology on the staff of the College of Physicians and Surgeons at Columbia University.

SOCIETY NEWS

Canadian Ophthalmological Society.—The annual meeting of the Canadian Ophthalmological Society will be held at the Chateau Laurier, Ottawa, Ontario, on Oct. 18 and 19, 1940. The subject of the scientific session will be "New Intravenous Drugs in Ophthalmology," under which the following topics will be discussed: anesthetics; pyretic drugs, including nonspecific protein and agents to produce shock; hypertonic solutions, including dextrose and sodium chloride; hemostatic drugs and anticoagulants; miscellaneous drugs, including substances opaque to roentgen rays, histamine, drugs for vital staining, vasodilators and acetylcholine; and blood transfusion.

Questions and Answers

FIBROSIS OF THE FLAP FOLLOWING TREPHINING

To the Editor:—I trephined an eye about three months ago for glaucoma. I took one suture in the conjunctiva for closure. Two days later when I removed the dressing I noticed that the conjunctiva over the hole was red and swollen and was encroaching on the cornea for about $\frac{1}{16}$ inch, forming a sort of blister. This swelling gradually enlarged and became lighter in color. Now it is almost white, is firm and seems to be attached to sclera and cornea.

What is the best way to remove this mass?

G. D. R., Louisiana.

Answer.—The mass of tissue at the site of the trephine is formed by proliferation of connective tissue in response to trauma or inflammation and involves the conjunctival and corneal epithelium. Such a reaction occurs more frequently in the Negro race but is by no means found solely there. The tendency to thickness of the flap with consequent closure of the trephine opening is one of the contraindications to a trephine operation for congestive or uncompensated glaucoma. In case the mass closes the fistula, permitting a rise of tension, it may be better to select another site for a second trephining or to employ some other type of operation.

In the absence of congestion the removal of the mass is optional. If it is large, it may be removed and the area covered by a conjunctival flap. The choice of method of making the flap depends on the way the original flap was made and the condition of the conjunctiva. The mass should be resected and the trephine opening covered either with some type of a finger conjunctival pedicle flap or with a sliding flap. A simple type of flap that can be made with a minimum of trauma will best serve the purpose. Sutures should not be placed near the fistula, as they are likely to be the means of bringing infection to the anterior chamber. A satisfactory method of removal of excess proliferative tissue about the trephine is as follows:

Induce anesthesia by injecting 1 cc. of a 2 per cent solution of procaine hydrochloride beneath the conjunctiva at the insertion of the superior rectus tendon. Incise the conjunctiva at the limbus above from 9 to 3 o'clock, making the line of incision just above the bleb so as to conserve as much conjunctiva as possible, and undermine the conjunctival epithelium so as to form a large free flap. With a sharp scalpel, remove the conjunctiva forming the bleb and all scar tissue about the trephine and the corneal epithelium 3 mm. from the trephine opening. Bring the flap forward over the cornea, anchoring it by sutures inserted at the limbus at 5 and 7 o'clock. (Remove the sutures on the sixth day.) Dress the eye daily, irrigating it with a warm solution of boric acid followed by the instillation of a solution of metaphen (1 : 2,500). Massage the eye several times daily, increasing the pressure as the soreness leaves and the tension requires.

SILVER ACETATE FOR PROPHYLAXIS AGAINST OPHTHALMIA NEONATORUM

To the Editor:—Some advice is being prepared for the physicians of Michigan pertaining to preservation of sight in children.

In the past they have been advised to use a 1 or 2 per cent solution of silver nitrate in the eyes immediately after birth. No mention was made of irrigation immediately after this medication.

Having read Dr. W. F. Hartman's report on his use of silver acetate in place of silver nitrate, as reported in the *Pennsylvania Medical Journal* (43: 639, 1940), I would appreciate your opinion of the same.

The use of silver nitrate has been in general satisfactory, and I know silver acetate at present is available in few drug stores. However, it could be supplied in ampules by the state, as is a large part of the silver nitrate solution now used for this purpose. The cost would be greater but not prohibitive.

Do you think the advantages would be sufficient to justify the difficulties involved in such a change of procedure?

G. H. B.

Answer.—With the Credé method of prevention of ophthalmia neonatorum it has been customary to use a 2 per cent solution of silver nitrate immediately after birth. Silver nitrate, when it breaks down, forms a double silver salt and nitric acid. Silver acetate breaks down into a double silver salt and acetic acid. Acetic acid is said to be less irritating to the eye than nitric acid, while the gonococcocidal powers of the two agents are equivalent in equal strength. Another objection to the use of silver nitrate is that a solution stronger than 2 per cent is likely to be irritating, and use of strong solutions has resulted in severe damage to the eyes. In contrast to this, silver acetate solution becomes saturated at 1.21 per cent, and the saturated solution is not irritating to the conjunctiva. The use of a solution of silver acetate would provide protection against ophthalmia neonatorum equal to that of a solution of silver nitrate and would avoid chemical conjunctivitis and the possibility of employing solutions too strong to be tolerated.

Silver acetate has been used as a substitute for silver nitrate in some hospitals for several years, but the limited number of demonstrative cases from which conclusions can be drawn is due to the excessive zeal of legislative action. The fact that Pennsylvania requires by authority of the health department, which is equivalent to law, the use of silver nitrate or other approved agents of like character in the eyes of all newborn children made the experimental use of silver acetate possible only with the permission of the state health department. This means a change of established routine in many hospitals, and the effort is simply not put forth to make these desirable experiments.

Abstracts from Current Literature

Bacteriology and Serology

CONSIDERATIONS ON ALLERGY. RAUL ARGANARAZ, Arch. de oftal. de Buenos Aires 14: 293 (April) 1939. OCULAR ANAPHYLAXIS AND ALLERGY. ibid. 14: 355 (May) 1939.

The first paper deals with allergy and anaphylaxis in general, allergy being considered the hypersensitivity acquired by the human organism to a large number of medicinal and alimentary substances, made apparent by divers clinical manifestations, such as sneezing, rhinorrhea, coryza, asthma, headache, cutaneous eruptions and itching, edema of the skin, diarrhea, constipation and vertigo.

The study of anaphylaxis has permitted a better comprehension of allergy. Anaphylaxis has been especially noted after sensitizing injections of toxins or different albuminous substances and is studied particularly in connection with serum allergy, the antigen producing the anaphylactic hypersensitivity being termed anaphylactogen and the antibody causing the anaphylactic shock, anaphylactin or anaphylactic antibody.

The hypersensitivity comprises both anaphylaxis and allergy, anaphylaxis being used to designate the reaction provoked experimentally in animals by the injection of albuminoid substances and allergy, the reaction observed clinically in man, the antigen in this case being called allergen and the antibody allergine. Both reactions can be brought about both actively and passively.

The general phenomena induced are studied by the author, who classifies them according to their induction through (1) the respiratory tract, (2) the digestive organs and (3) the skin and (4) by injection.

The production of these phenomena by different foodstuffs, drugs, pollens, cutaneous infections and physical agents and their diagnosis by scarification of the skin, intradermal injection and ocular and nasal reactions are considered.

Once the diagnosis is established, a cure can be effected by suppression of the exciting cause, by desensitization, by autovaccination or by drugs, such as epinephrine, ephedrine, atropine, belladonna and morphine.

The second paper is mostly devoted to ocular allergy, knowledge in this field being initiated by the study of hay fever.

Ocular anaphylaxis was from the first studied experimentally, all the ocular membranes being exquisitely sensitive and easy to observe. For many years Elschnig alone explained the inflammatory lesions of sympathetic ophthalmia as anaphylactic phenomena, this fact today being almost universally accepted.

After a general study of the different ocular anaphylactic phenomena, Arganaraz considers them in detail in connection with conjunctival

allergy in hay fever, spring catarrh, parenchymatous keratitis, phlyctenular ophthalmia and phacoanaphylactic inflammatory lesions consecutive to traumatisms of the lens.   C. E. FINLAY.

Biochemistry

A STUDY OF THE CHEMICAL AND PHYSIOCHEMICAL TOPOGRAPHY OF
    THE LENS. E. TRON, Vestnik oftal. 14: 6, 1939.

This article reports the results of thorough experimental work done on the lenses of bulls' eyes. The investigation was divided into three parts: (1) a study of the morphologic structure of salt cataract, (2) a comparative chemical examination of various layers of the lens and (3) a study of permeability of the anterior and posterior capsules of the lens.

Salt cataract was produced by immersing a lens in hypertonic Ringer-Locke solution and in a solution of copper sulfate. The initial period of lenticular opacities produced by the first solution was characterized by a loss of water by the lens. The formation of a number of large vacuoles on the anterior surface of the lens was observed, while on its posterior surface a few small, swiftly disappearing vacuoles were noticed.

An accumulation of water (mostly on the anterior surface) under the capsule with absorption of the opacities was observed in the later period. The absorption was going on faster on the anterior surface than on the posterior surface. The opacities produced by immersion of the lens in the copper sulfate solution were due to precipitation of the proteins of the lens. The opacities were noticed on the posterior surface immediately after immersion; this surface was covered with linear opacities directed toward the center, while on the anterior surface the small punctate opacities were appearing slowly. The presence or absence of the lens capsule influenced the time and the morphologic form of the opacities. Thus it was established that the loss of water in hypertonic solution and the precipitation of the lens proteins by salts of copper had a different course on both surfaces of the lens.

The chemical study of the water and potassium of the various layers of the lens gave the following results: The average content of water equaled 70.7 per cent in the anterior cortical layer and 72 per cent in the posterior cortical layer. The potassium content (in milligrams per dry weight) was as follows: 1.069 in the anterior cortical layer and 1.222 in the posterior cortical layer; in the nucleus it was 0.663. This content of water and of potassium is different in the anterior and in the posterior cortical layer.

Examination of the permeability of the lens capsule to salts showed that the permeability of the posterior capsule was much higher than that of the anterior capsule.

The conclusions are as follows:

1. The reaction of both surfaces of the lens to the influence of equal external factors is different.

2. The chemistry of the anterior and of the posterior cortical layer is not the same.

3. The anterior and the posterior lens capsule possess a different permeability.

Tron believes that no definite conclusions can be made but that further studies of the physiochemical topography of the lens will give valuable data for the understanding of the pathogenesis of cataract.

Eleven tables illustrate this article fully.   O. Sitchevska.

Conjunctiva

Erythema Nodosum with Nodules in the Conjunctivae. L. S. Greene and M. W. Perry, Am. J. Ophth. 22: 389 (April) 1939.

Greene and Perry report the case of a 54 year old woman who presented triangular, cherry red areas in each eye over the insertions of the rectus muscles. These injections were confined to the bulbar conjunctivas, and within these areas were from two to four nodes the size of a small pinhead. Five days later fever, general malaise, pains and redness of the joints and pharyngitis developed. Over the extensor surfaces of the arms and legs below the elbows and knees were typical nodules of erythema nodosum.   W. S. Reese.

Cornea and Sclera

Transplantation of the Cornea. José A. Sená, Arch. de oftal. de Buenos Aires 14: 385 (May) 1939.

After general remarks on transplantation of the cornea and its up-to-date development, the author reports a case in which the corresponding portions of the opaque and transparent corneas were excised with Franceschetti's trephine, the transplant being maintained in position by means of a large conjunctival flap everted from the upper corneal margin and sutured to the inferior corneal circumference. The transplanted cornea came from an eye with an orbital sarcoma.

C. E. Finlay.

Blue Sclera Combined with Abnormal Fragility of the Bones and Deafness (Adair-Dighton's Syndrome). H. Rose, Arch. f. Ophth. 140: 278 (April) 1939.

The syndrome of blue sclera, abnormal fragility of the bones and deafness should be named after Adair-Dighton (*Ophthalmoscope* 10: 188, 1912), the first person to describe it. Rose reports the pedigrees of 3 families, in each of which several members of different generations showed this syndrome. The mode of transmission was of the dominant type. The disease is discussed in the light of the new German laws, which aim at the elimination of hereditary diseases.

P. C. Kronfeld.

Experimental Pathology

Alterations in Response to Visual Stimuli Following Lesions of Frontal Lobe in Monkeys. M. A. Kennard, Arch. Neurol. & Psychiat. 41: 1153 (June) 1939.

Previous investigations on the functions of the frontal lobes in monkeys showed that the animals from which an entire frontal lobe had

been removed did not appear to see objects in the contralateral field of vision. The present study localized the exact cortical area responsible for these visual changes. By making a series of small discrete lesions involving only the gray matter of the cerebral cortex it was possible to identify an isolated area, ablation of which was constantly followed by this unilateral visual defect. Extirpation of area 8, a small region lying inside the curvature of the arcuate sulcus, was invariably followed by failure to respond in a normal manner to objects placed in the contralateral visual field. The defect in vision could not be distinguished from the true hemianopia following amputation of one occipital lobe. However, the defect was not a true hemianopia since it was only transient, appearing immediately after operation and disappearing gradually in the succeeding weeks. The defect was always accompanied by conjugate deviation of the head and eyes to the side of the lesion. The latter symptoms were also transient and disappeared before the visual defect. There was no associated paresis, and gait, posture and fine movements of prehension were normal.

Bilateral extirpation of this area resulted in an animal not actually blind, since at times the eyes followed moving objects or a light, but an animal not recognizing objects as judged by the lack of normal protective response against hand movements that would ordinarily cause blinking and withdrawal and the lack of normal response to the presentation of food. The abnormality of behavior was apparently of the same order as that of the apraxic patient.   R. IRVINE.

CHEMOTHERAPEUTIC ACTION OF SULFANILAMIDE IN EXPERIMENTAL OCULAR INFECTIONS.   L. VENCO, Ann. di ottal. e clin. ocul. 67: 179 (March) 1939.

Dilutions of a virulent strain of Streptococcus haemolyticus were injected into the anterior chamber of rabbits. The administration of sulfanilamide was begun the day of the inoculation or on the following day. Fifteen animals were employed. With the strain of streptococcus employed, 0.1 cc. of a 1 : 100,000 dilution produced in controls an active infection ending in panophthalmitis, the rapidity of the process showing some variation. While a few conflicting facts were observed, in general the animals receiving the drug showed a resistance to much higher doses of the streptococcus, in some cases 0.1 cc. of a 1 : 500 dilution. This was observed only when the doses of drug were large and frequently repeated. With these doses some exudate appeared in the anterior chamber, often obstructing the pupil, but the infection remained localized and gradually subsided. One animal treated with small doses and a control died of septicemia. Variations in the course of infection, even in the treated animals, were ascribed to differences in natural resistance. In some animals in which the infection appeared to be arrested by treatment, stopping the administration of the drug resulted in an immediate aggravation of the process, which developed into panophthalmitis. Various theories as to the action of the sulfanilamide group of drugs are reviewed. In the author's experiments, a dose of the drug 0.1 Gm. per kilogram of body weight showed a protective effect against 0.1 cc. of a 1 : 10,000 dilution of the streptococcus, while 0.5 Gm. of the drug per kilogram showed a similar effect against concentrations as high as 1 : 500.

S. R. GIFFORD.

METABOLISM OF THE RETINA IN AVITAMINOSIS. F. DE LEONIBUS, Ann. di ottal. e clin. ocul. **67**: 512 (July) 1939.

The chemistry of visual purple and its derivative, retinene, is reviewed. In the author's experiments, albino rats were placed on a vitamin A–free diet until many showed signs of keratomalacia. The retinas were removed and placed in a Warburg respirator, the retina of a control animal being submitted to the same technic with that of each avitaminotic animal. No difference was found in oxygen consumption between the two groups of animals. The glycolytic power, however, was constantly higher in the retina of the avitaminotic animals, the average increase above normal being 8.6 per cent. S. R. GIFFORD.

General Diseases

THE SIGNIFICANCE OF THE B VITAMINS IN OPHTHALMOLOGY. S. VON GRÓSZ, Arch. f. Ophth. **140**: 149, 1939.

The history, chemistry and physiology of vitamin B_1 are briefly reviewed, following closely the papers by Williams (The Chemistry of Thiamin [Vitamin B_1], *J. A. M. A.* **10**: 727 [March 5] 1938) and Cogwill (The Physiology of Vitamin B_1, ibid. **110**: 805 [March 12] 1938) and the monograph by Stepps and his associates (in German). The population of Hungary probably has an insufficient intake of vitamin B_1, because the food is poor in fats and proteins and rich in carbohydrates, most of which are consumed in the form of white bread. Measures to encourage more extensive consumption of milk and vegetables and of more bran-containing bread are under way. Severe vitamin B_1 deficiency leads to beriberi, whereas the milder degrees manifest themselves in the form of mild polyneuritis and gastrointestinal disturbances on the order of lowered secretory and motor function. Thereby the absorption of vitamin B_1 from the food is made worse, and a vicious cycle is established. The development of the concept that alcoholic polyneuritis is a disease due to vitamin B_1 deficiency is given in detail. To Dr. Carroll, of New York, goes the credit for having introduced the treatment of alcohol-amblyopia with vitamin B_1 (Analysis of Fifty-Five Cases of Tobacco-Alcohol Amblyopia, ARCH. OPHTH. **14**: 421 [Sept.] 1935; "Alcohol" Amblyopia, Pellagra, Polyneuritis, ibid. **16**: 919 [Dec.] 1936; Importance of Diet in the Etiology and Treatment of Tobacco-Tobacco Amblyopia, ibid. **18**: 948 [Dec.] 1937). The author of the paper under review reports 15 cases of alcohol-tobacco amblyopia; after three weeks of complete abstinence, the patients were treated with large doses of vitamins B_1 and B_2. After four to six weeks of such treatment, 6 patients were cured and 3 had improved. The condition of the other 3 had remained stationary. After the three weeks of abstinence, 3 of the cured and 1 of the improved patients resumed drinking and smoking but remained on a diet rich in all B vitamins. The amblyopia did not recur. The author states that it would be interesting to study the intake and output of vitamin B_1 in cases of alcoholic polyneuritis. The retrobulbar neuritis which occurs during pregnancy or lactation should be considered as a manifestation of vitamin B_1 deficiency and be treated accordingly. In multiple sclerosis,

injections of vitamin B_1 may be tried. In tabetic atrophy of the optic nerve treatment with vitamin B_1 has been tried without definite results. Atrophy of the optic nerve which occurs in pernicious anemia seems to respond favorably to treatment with this vitamin.

Vitamin B_1 is a strong analgesic and may be used advantageously in the treatment of neuralgia, herpes zoster and gout.

Vitamin B_2 deficiency is, at least in Europe, much less common than vitamin B_1 deficiency. The work of Day, Langston and O'Brien (*Am. J. Ophth.* **14**: 1005, 1931) on experimental cataract produced in rats by a diet deficient in vitamin B_2 and its various ramifications is reviewed.

                                                            P. C. KRONFELD.

OCULAR TUBERCULOSIS AND BENIGN LYMPHOGRANULOMATOSIS: REPORT OF CASES. F. W. MEYER, Klin. Monatsbl. f. Augenh. **102**: 76 (Jan.) 1939.

Meyer refers to his view expressed in a previous paper on "Lymphogranulomatosis and Iridocyclitis" (*Klin. Monatsbl. f. Augenh.* **100**: 76 [March] 1938). These views were questioned at a meeting of the Deutsche Ophthalmologische Gesellschaft in Heidelberg in 1938. In the present paper the author publishes 2 case reports in support of his views. The cases concern cutaneous lesions known as benign lymphogranulomatosis, Boeck's sarcoid and multiple benign miliary lupoid. The first case is that of a woman aged 25 and the second that of a man aged 24. Pieces of epidermis were excised for histologic examination in each case. Genuine ocular tuberculosis existed in the first case and stubborn iridocyclitis in the second. The ocular disease occurring in association with benign lymphogranulomatosis is of a tuberculous nature. This is evidenced by the clinical course and the tendency of benign lymphogranulomatosis to produce secondary phthises of the organism. Typical efflorescence in the skin, described by Schumann, cystic osteitis, described by Jüngling, and in addition, involvement of large groups of lymph vessels and typical roentgenographic changes in the lungs coupled with enlargement of the mediastinal lymph glands complete the picture of lymphogranulomatosis. Complicating ocular disorders present the appearance of genuine ocular tuberculosis in a number of cases. The tuberculin test is negative during full development of the disease. The importance of the roentgenogram of the lungs is questionable, and the peculiar findings in the lungs prevent classifying them as some certain type of tuberculosis. Only histologic examination may establish the diagnosis of the cutaneous eruption. Benign lymphogranulomatosis very likely represents an atypical form of tuberculosis.   K. L. STOLL.

Glaucoma

MANAGEMENT OF GLAUCOMA FOLLOWING CATARACT OPERATION. B. Y. ALVIS, Am. J. Ophth. **22**: 518 (May) 1939.

Alvis enumerates and discusses the causes of glaucoma following cataract operations and concludes that they are usually the result of a fault in technic. The prevention and treatment are then taken up, and several illustrative cases are reported.   W. S. REESE.

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The Treatment of Glaucoma with Splenic Extract. E. A. Miller, Am. J. Ophth. 22: 536 (May) 1939.

Miller draws the following conclusions after the use of splenic extract in cases of glaucoma:

"1. Primary glaucoma is an angioneurotic edema within the eyeball, just as migraine is an angioneurotic edema of the brain. This is proved by the prompt relief of symptoms and reduction of intraocular pressure following the injection of a deproteinized extract of hog spleen.

"2. The only reaction to be feared from this treatment is an intensification of symptoms, sometimes following an injection. Such reactions have been observed in cases of asthma, angioneurotic edema, urticaria, and eczema.

"3. Continuation of this treatment will result in permanent recovery in most cases.

"4. The danger of opening the eyeball under high tension is greatly reduced in cases demanding operation despite this treatment.

"5. Therapeutic effects are not in proportion to the degree of the splenic extract's concentration, and favorable results can be obtained only if the extract happens to contain the curative element.

"6. There is a crying need for laboratory investigation which might discover the physiologic action of this remedy, as well as a means of biologically standardizing it."   W. S. Reese.

Tonometry and Unusual Cases of Glaucoma. E. Jackson, Am. J. Ophth. 22: 614 (June) 1939.

Jackson warns against too much dependence on tonometry in the diagnosis of glaucoma and the idea that increased intraocular pressure means glaucoma. He cites cases showing that blindness may not be inevitable, even in cases in which treatment is not given, and that increased tension may be present for a time without any danger of glaucoma.   W. S. Reese.

Prepapillary Proliferation of Connective Tissue in Glaucoma and Its Relation to Retinitis Proliferans. M. Salzmann, Arch. f. Ophth. 139: 629, 1939.

On histologic examination the glaucomatous excavation is usually found to be empty. Its floor is formed by a thin and compressed-looking layer containing nerve fibers and neuroglia. In certain phases of glaucoma this layer may become edematous and fill the excavation—in which case the histologic picture of the tissues inside the excavation resembles that of cavernous atrophy of the optic nerve. This edema of the prelaminar tissues in glaucoma is usually only a transient phase. The prepapillary connective tissue proliferation in glaucoma is an entirely different pathologic condition. It is located anteriorly to the glia lining of the excavation and to the inner limiting membrane of the retina if it extends onto the retina. It is made up of collagenous connective tissue without definite fibrillar structure and resembles myxomatous tissue. It contains few cells and has a pronounced tendency to shrink once it has reached a certain

stage of development. This shrinking tends to pull the retina into the excavation. A characteristic feature of prepapillary connective tissue proliferation is the fact that it contains numerous newly formed vessels which anastomose with retinal vessels.

The prepapillary connective tissue proliferation is found in eyes with far advanced, primary or secondary glaucoma. A constant finding in these eyes is degeneration of the retinal vascular system in the form of obliteration of capillaries, of sclerosis of the walls of the larger vessels and of complete or partial venous obstruction. Leber expressed the belief that prepapillary connective tissue proliferation represents the result of organization of prepapillary hemorrhages. Salzmann is of the opinion that it is often associated with retinal or prepapillary hemorrhages but that its real cause is the vascular disturbance in the retina which through alterations of the normal metabolism gives rise to a plastic inflammatory process. The same mechanism may apply to the true retinitis proliferans. "I have shown that obstruction of the central vein may be the cause as well as the result of glaucoma. The same applies to retinitis proliferans which may lead to secondary glaucoma or occur as a sequela of primary or secondary glaucoma. . . . Obstruction of the central vein plays an intermediary part in both pathologic mechanisms." P. C. KRONFELD.

Injuries

LOCALIZATION OF AN IRON SPLINTER LODGED IN THE RETINA BY CATHOLYSIS WITH DIASCLERAL REMOVAL BY THE HAND MAGNET. H. SCHEYHING, Klin. Monatsbl. f. Augenh. 102: 540 (April) 1939.

An iron splinter entered the eye of a man aged 21 through the cornea and lens. It was observed about 6 disk diameters below the optic nerve. Several attempts with the giant magnet failed to dislodge the splinter. Three punctures were done with the catholysis needle. The foam arising from one puncture could be observed with the ophthalmoscope in close proximity to the splinter. The sclera was incised after Mendoza's method, sparing the choroid, and the splinter was extracted with the hand magnet. A small portion of vitreous was abscised, the wound was closed and the inferior rectus muscle, which had been detached temporarily, was reattached. K. L. STOLL.

Lens

PRESENCE AND SIGNIFICANCE OF VITAMIN B_1 IN THE CRYSTALLINE LENS. F. P. FISCHER, Arch. d'opht. 2: 108 (Feb.) 1938.

Fischer on the basis of a series of observations shows first that the normal lens contains no thiochrome; second, that it contains vitamin B_1; third, that the vitamin B_1 content of the lens is 0.001 microgram, and fourth, that a cataractous lens contains no vitamin B_1. The relation between pyruvic acid and vitamin B_1 is such, according to de Jong, that when vitamin B_1 is deficient pyruvic acid accumulates. Fischer presents two tables showing the percentage of this acid in beef and calf lenses and from these concludes that neither weight nor age has any influ-

ence. He then presents a table showing the percentage of pyruvic acid in 10 cataractous lenses extracted in capsule. In all there was an increase in pyruvic acid. A second group of 12 lenses extracted in capsule showed that the denser the cataract the greater the content of pyruvic acid. These findings were rechecked in a second group of 20 lenses. As a result of these observations, Fischer concludes: (1) that faulty metabolism of the glucocides plays an important role in the pathogenesis of cataract; (2) that it is characterized by an incomplete reduction of pyruvic acid into lactic acid, and (3) that it is due to the disappearance of vitamin B_1 in cataract.   S. B. MARLOW.

VITAMIN C METABOLISM OF PATIENTS WITH CATARACT: REPORT OF CASES. J. URBANEK, Klin. Monatsbl. f. Augenh. 101: 670 (Nov.) 1938.

The author showed in a previous paper (*Ztschr. f. Augenh.* 95: 128, 1938) that postoperative hemorrhages in the anterior chamber of patients with cataract are due in most cases to a lack of vitamin C or to relative avitaminosis C and that these hemorrhages can be prevented in most instances by saturation and with vitamin C. This paper deals with a continuation of Urbanek's research, the results being recorded in the tables. The standard of saturation in all cases was judged by the excretion in the urine. The tables show the results in juvenile patients with ocular diseases; in patients with cataract who had retarded elimination of urine and in patients with cataract and normal elimination. There are also tables containing data on the vitamin C metabolism of patients with inflammation of the eyes; of patients with cataract, observed in 1937 and 1938; of patients with aphakia, and of patients with cataract complicated with myotonia, megalocornea, heterochromia and iritis.

The results of this most detailed research follow: The lens is not responsible for the quantity of vitamin C in the anterior chamber. Seasonal variations of vitamin C content in the blood serum, in the aqueous humor or in the lens could not be found. The ages of the patients with cataract were irrelevant, as demonstrated in the tables. The content of vitamin C in the blood serum, the aqueous humor and the lenses of patients with cataract and heterochromia did not vary from that of patients with uncomplicated cataracts, although the inflammatory symptoms had existed for several years (table 10).

Urbanek arrived at the following conclusions:

1. The juvenile organism is better provided with vitamin C than the senile organism.

2. The formation of cataract in aged patients is not always dependent on avitaminosis. Well nourished patients with cataracts presented vitamin C contents similar to those of juvenile persons.

3. The inferiority of vitamin C in senile persons does not allow the conclusion that the development of a cataract is the result of avitaminosis C.

4. The uniformity of ascorbic acid in the aqueous humor, which is independent of the saturation of the organism, indicates that the deficiency of vitamin C in the aqueous humor develops much slower than

in the blood serum. On the other hand, it is probable that an increase of vitamin C will occur slower in the aqueous humor than in the blood serum.

5. The lens is neither necessary nor responsible for the formation of vitamin C in the aqueous humor.

Further research on juvenile persons without cataract is expected to show whether it will be possible to prevent the formation of a cataract in a person of advanced age by saturation with vitamin C. The author's attempts at preventing the formation of a cataract in the second eye had been futile up to the time his report was written. Consideration will also be given to the class of persons who are more subject to the formation of cataract as a result of a vegetarian diet. Favorable influences on the psyche and the organism were observed which are supposed to retard the formation of cataract if treatment with vitamin C can be begun before the lenticular opacities cause a disturbance.

<div align="right">K. L. Stoll.</div>

Methods of Examination

Contribution to the Theory and Practice of Tonometry. J. S. Friedenwald, Am. J. Ophth. 22: 375 (April) 1939.

Friedenwald reviews the work of Kalfa on tonometry with the Maklakow tonometer and compares it with his own observations with the Schiötz instrument. He concludes that it is possible to apply to Kalfa's elastometric measurements with the applanation tonometer the same type of analysis that he applied to data obtained with the Schiötz tonometer and that results of both methods are capable of confirming and supporting each other.

<div align="right">W. S. Reese.</div>

Ophthalmoscopy Through the Hazy Cornea in Glaucoma. S. Larsson, Acta ophth. 17: 297, 1939.

The author observes that it does not seem to be generally known that the hazy cornea of a glaucomatous eye can be temporarily clarified by a simple method. After the instillation of pontocaine, strong uniform pressure is applied to the center of the cornea by means of a glass rod with a spherical end 3 or 4 mm. in diameter. Pressure should be so strong that the cornea is indented and should last for from thirty to sixty seconds. The "pressure spot" remains clear long enough for ophthalmoscopic examination to be performed through it.

<div align="right">O. P. Perkins.</div>

Neurology

Introductory Essay on the Study of the Paths and Centers of the Conjugate Movements of the Eyes. G. E. Jayle, Arch. d'opht. 2: 401 (May) 1938.

Jayle points out that the consideration of the conjugate movements of the eyes is still dominated by the scheme of Grasset and Landouzy in spite of many criticisms and recent work. He briefly sets forth this scheme. In the last analysis there are three postulates about the move-

ments which must be taken into consideration: (1) the physiologic identity of the ocular movements to somatic movement; (2) the preeminence of the cortical influx, voluntary or not, on the subcortical influx in the central oculogyric regulations, and (3) the physiologic identity of three fundamental types of movements associated with them.

Jayle points out that while the first of these hypotheses has been admitted and can be demonstrated by experiments which affect certain parts of the cortex, no lesions of a paralytic nature are known to exist from the destruction of the cortex. In support of this he points out the case in which Dandy removed a hemisphere and also a case of glioma reported by Guillain. There is considerable discussion of the ocular movements in relation to equilibrium. The second hypothesis Jayle finds difficulty in accepting, and the evidence in support of his contention is presented. The third hypothesis is discussed in relation to the stimulation of the semicircular canals. The observation of the slow component rather than of the quick component and the resulting nystagmus is made. In his conclusions he lays emphasis on the importance of the subcortical factors in the regulation of conjugate movements. This article should be read in the original.

S. B. Marlow.

Electric Examination of the Occipital Region in Lesions of the Optic Pathways (Modifications of Berger's Rhythm). A. Baudouin, P. Helbron, H. Fischgold and R. Y. Mion, Bull. Soc. d'opht. de Paris **51**: 176 (March) 1939.

The authors review in a simple manner the investigations of Berger and those others who have demonstrated methods of obtaining electric discharges from the region of the occipital lobe.

The discharge. has confined itself to two different types of waves. The alpha waves produced at a frequency of 8 to 10 per second have an amplitude between 30 and 120 millivolts, are exceedingly regular with regular increase and decrease when taken from the occipital region. The beta waves have a constancy over the entire surface of the cranium. and their oscillations are more frequent, from 17 to 60 per second. and vary greatly. Their amplitude is a feeble one, being in the neighborhood of 10 millivolts. They are unstable and irregular. In the phenomenon called reaction of the arrest of Berger's rhythm, if the eyelids are open the visual stimulation stops the alpha waves and replaces them by beta waves. This arrest also occurs if the person is trying to see with the lids closed and also if another sensory nerve is stimulated, such as the auditory. The beginning of the arrest is known as the "on effect," and its termination is called the "off effect."

The authors have made observations on some patients with various types of lesions of the optic pathways and report their findings. The first was a totally blind woman. The alpha rhythm existed with a rate of 7 to 8 per second. The amplitude was only 33 millivolts. There was no phenomenon of arrest. The alpha wave was more feeble in the occipital region than in the precentral, being the inverse of the normal.

Neurologic examination of the second patient, who had right homonymous hemianopia and a left lower quadrant anopia, gave nega-

tive results. The alpha frequency was infrequent, only to 2 to 10 per second for either side, and there was no arrest phenomenon.

The third patient had hemianopia, preservation of macular vision and tubular fields. Neurologic examination gave negative results, and the phenomenon of arrest was very positive, with a rhythm of 10 per second and feeble amplitude.

The fourth patient had bilateral central scotomas and normal fundi and pupils, with greatly reduced vision. A probable diagnosis of opto-chiasmic arachnoiditis was made. The rhythm was 8 per second, the amplitude was 50 millivolts, and there was a positive arrest phenomenon.

The authors conclude:

1. Blindness causes diminution of amplitude and absence of "on effect."

2. The phenomenon of arrest is bound up with the preservation of central vision.

3. The correlation of the physiologic findings and the psychic phenomenon will aid in the solution of the problem.   L. L. MAYER.

RARE TYPES OF INTRACRANIAL COMPRESSION OF THE OPTIC NERVE. G. P. SOURDILLE and M. DAVID, Bull. Soc. d'opht. de Paris 51: 183 (March) 1939.

Two cases of intracranial compression of the optic nerve of a rare type are reported. The first is that of a patient of 45 years of age who complained of attacks of blindness for one or two minutes accompanied by headache. During one of the severe attacks the vision of the right eye was reduced to ability to count fingers at 30 cm., while the left had no perception for light. Both pupils were widely dilated, the right only reacting to light. The papillae were pale, with soft outlines. The arteries were thin. The initial diagnosis was one of vascular spasm. Roentgenograms of the sellar region showed effacement of the clinoid processes, a cloudy bone and effacement of the left sphenoid wing. At operation swelling of the optic nerves with a moderate arachnoiditis was noted.

The second patient, aged 73, consulted an ophthalmologist because of cataracts. Visual acuity of the right eye was 0.1 and of the left 0.3. Opacities of the lenses were not enough to account for the poor vision. The papillae were pale, with blurred borders. The tension and the macular areas were normal. The left visual field was normal, but the right showed a concentric contraction with predominence in loss of the inferior half. Roentgenograms were negative. Pneumonia developed, and the patient died. Autopsy revealed an atheroma of the carotid artery pressing on the optic nerve.   L. L. MAYER.

Orbit, Eyeball and Accessory Sinuses

GUMMA OF THE ORBIT. M. FINE, Am. J. Ophth. 22: 595 (June) 1939.

Fine reports 2 cases of gumma of the orbit in Negresses aged 37 and 27. He calls attention to the rarity of this disease and enumerates the symptoms. His 2 cases represent the two anatomic groups, namely,

those involving the apex and those involving the margins of the orbit. He recommends potassium iodide and compounds of one of the heavy metals for treatment and urges that in therapeutic diagnosis the treatment be continued for at least one month and that adequate potassium iodide (40 to 100 grains [2.6 to 6.5 Gm.] daily) be given.

W. S. REESE.

PSEUDOTUMOR OF THE ORBIT. E. DALSGAARD-NIELSEN, Acta ophth. **17**: 418, 1939.

The author reports 2 cases of orbital pseudotumor. The first was that of a girl of 19. There were no positive findings other than 3 mm. of proptosis of the right eye and a firm and freely movable mass which was palpable through the lower eyelid. On removal, this proved to be composed of nonspecific, chronic, inflammatory tissue.

In the second case progressive exophthalmos of the right eye developed in a woman of 70. In the belief that a malignant tumor was present exenteration of the orbit was done. The pathologic diagnosis was chronic dacryoadenitis spreading into the orbit. O. P. PERKINS.

Pharmacology

EFFECT OF VARIOUS CONCENTRATIONS OF PILOCARPINE ON INTRAOCULAR TENSION. S. I. ROSSEL, Vestnik oftal. **15**: 48, 1939.

The absorption of pilocarpine is swiftest when the solution is hypertonic, at a p_H of from 7.4 to 7.6. A 6 per cent solution of pilocarpine was found to meet these requirements on experimental investigation. Rossel used pilocarpine in a 1 to 6 per cent dilution on 78 eyes affected with chronic, simple, inflammatory and absolute glaucoma and also on a few normal eyes. The use of a high concentration of pilocarpine caused no complications. Several diagrams illustrate the article.

Rossel draws the following conclusions :

1. Pilocarpine in high concentration does not influence the tension in a normal eye.

2. A 0.5, 1 and 2.3 per cent solution of pilocarpine has about the same action on glaucomatous eyes.

3. A 6 per cent solution of pilocarpine has the advantage over a 1 per cent solution in that it is sufficient to instil it only once or twice in order to keep the intraocular tension down for a long time.

O. SITCHEVSKA.

Retina and Optic Nerve

SUDDEN BLINDNESS. JOSEPH MINTON, Brit. M. J. **2**: 61 (July 8) 1939.

After reviewing the vascular causes of sudden blindness and describing the three phases of hypertension in the retinal vessels (Dumas, Wagener and Keith), the author reports on the result of his investigation of patients at the Royal Ophthalmic Hospital in London from 1931 to 1936. During this period 205 cases of thrombosis of the retinal vein or

its tributaries were observed, while only 54 cases were seen in which there was occlusion of the retinal artery or of one of its branches. A number of the patients with closure of the central retinal artery, which the author considers in the vast majority of instances to be due to localized thrombosis in spastic and thickened arteries in association with hypertension, remained in good health for many years. One half of them were alive several years after the onset of the sudden blindness. This suggests that the arteriolar sclerosis follows a patchy and irregular distribution and that the involvement of the retinal arteries does not indicate disease of the cerebral or coronary vessels in all cases. For the treatment of these closures, the author recommends subconjunctival injections of acetylcholine, inhalations of amyl nitrite, the use of glyceryl trinitrate and massaging of the eye and in cases in which the condition is grave, paracentesis.

A case is reported in which a patient 54 years of age had sudden loss of vision in the right eye and presented a typical picture of a closure of the retinal artery. His blood pressure was 180 systolic and 100 diastolic. Inhalations of amyl nitrite were ordered, and the eye was massaged without effect. A subconjunctival injection of acetylcholine (5 minims [0.31 cc.]) was given and was followed within one-half hour by a gradual return of sight. A second subconjunctival injection of the same amount of acetylcholine was given after three hours. The following day the vision was 6/18, but the defect of the inferior nasal sector was permanent.

The author concludes that attacks of sudden blindness should be regarded as a warning of vascular disease. In the diagnosis and prognosis, the study and correct interpretation of the accompanying retinal changes are essential. ARNOLD KNAPP.

FORMATION OF HOLES IN THE CENTER OF THE RETINA: REPORT OF CASES. R. SCHMIDT, Klin. Monatsbl. f. Augenh. 102: 521 (April) 1939.

The importance of rupture of the retina in the detachment of the retina is known. Holes in the macula make an exception. They rarely lead to detachment and yield unsatisfactory results when operated on. Schmidt reports 14 cases in point in which the patients ranged in age between 8 and 56 years. The cause of the detachment in 6 of these cases was trauma, which had occurred a long time previously. In 1 patient who was seen the day after the detachment senile changes were noted in the macula, which may have favored the formation of a central retinal tear. The author discusses the mechanism of the formation of holes in the macula, adding the points of differential diagnosis between holes and cysts. He found that no detachment occurred in 9 of his 14 patients with holes in the macula, or that it remained limited to within the fovea centralis; 8 of these 9 patients remained under observation for months and years, during which time the fundus was practically unchanged and vision did not grow worse. Operative procedures, therefore, are not considered in such cases at the Ophthalmic Hospital of Freiburg.

K. L. STOLL.

Trachoma

OBSERVATIONS ON THE CULTURE OF TRACHOMATOUS TISSUE BY THE CARREL METHOD AND COMMENTS ON THE WORK THAT HAS APPEARED ON THIS SUBJECT. A. BUSACCA, Arch. d'opht. 2: 116 (Feb.) 1938.

Busacca calls attention to the disagreement in the results of the work of Harrison and Julianelle and Poleff and Thygeson. The difficulties in technic are pointed out. The author's own procedure is described. He calls attention to the degenerative changes in the centrosphere demonstrated by Lewis and Webster and expresses his opinion that at least some of the formations described in the literature as Prowazek bodies must be related to the changes in the zone about the centrosphere. While a study of living cultures alone can lead to the demonstration of the vitality and multiplication of the bodies which he has interpreted as rickettsias, he points out that a large number of the cellular granules, normal or pathologic, can be mistaken for rickettsias. He reiterates his opinion that the endo-ocular nodules following intraocular inoculation must be considered nonspecific reactions.   S. B. MARLOW.

NEW POINTS OF VIEW IN CONTEMPORANEOUS EXPERIMENTAL STUDIES OF TRACHOMA. M. POLEFF, Arch. d'opht. 2: 517 (June) 1938.

Poleff reviews the recent experimental work which has been done on trachoma and shows that one of the greatest obstacles that has been overcome is the ability to inoculate the organism of trachoma in animals and then to produce other lesions. As a result of the work of Cuénod and Nataf, the causal organism in trachoma has been classified as possibly Rickettsia, rocha limae. In order to settle the question, he believes that the experimental inoculation of man with this culture is absolutely indispensable. He believes that further experimental evidence is necessary through the culture of the virus in question. Up to the present the results of experiments with pure cultures makes the probability of its etiologic role likely.   S. B. MARLOW.

Vitreous

CLINICAL PICTURE OF DETACHMENT OF THE VITREOUS. J. FRONIMO-POULOS, Arch. f. Ophth. 140: 482, 1939.

The work of Lindner, Pillat, Sallmann and Rieger on detachment of the vitreous is reviewed (*Arch. f. Ophth.* 133: 75, 1934; 135: 332 and 462, 1936; 137: 157, 1937). Twenty-six myopes with retinal detachment in one eye were examined for detachment of the vitreous with the slit lamp and the angulated corneal microscope of Lindner. In 25 eyes with retinal detachment and in 21 eyes without retinal detachment the vitreous was found to be detached from the retina. In another series comprising myopes with and without retinal detachment and patients with tapetoretinal degeneration or with senile degeneration of the fundus, the changes in the extent of detachment of the vitreous occurring during periods varying from four months to five years were studied. In the cases of persistent retinal detachment, progression of the detachment of the vitreous was most common and most pronounced.
          P. C. KRONFELD.

Society Transactions

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ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY

C. S. O'BRIEN, M.D., *Secretary-Treasurer*

Eleventh Scientific Meeting, New York, June 11, 1940

Keratoconus Relative to the Effect of Prolonged Application of Pressure. DR. T. L. TERRY and DR. JULIAN F. CHISHOLM, Boston.

In an effort to determine why prolonged pressure on keratoconus is successful in reducing the deformity in some instances, a survey of the development, growth and histologic structure of the cornea, together with a study of the frequency, etiologic factors and pathologic picture of keratoconus, was made.

When the cornea first appears in embryonic life its radius is some 0.4 mm. It not only must grow in size and thickness but must become less curved.

From the time of its origin, the human cornea is thicker at its periphery than at its center. This thickness depends on a greater number of deeply placed lamellae which play out centrally by ending obliquely against Descemet's membrane. Even more superficially, the lamellae do not reach entirely across the cornea.

The substantia propria not only depends on white fibers for its tenacity but on a number of elastic fibers, which contribute more to its strength when the cornea is stretched.

Clinically insignificant keratoconus appears to be relatively frequent. In persons with 3 or more diopters of astigmatism, especially if one axis of the correction is myopic, careful study of the shape of the cornea will reveal many instances of mild keratoconus. This condition is especially likely to occur in patients who appear to have unilateral keratoconus.

Heredity appears to be a definite factor only in some cases. When a hereditary basis is evident, Mann considers keratoconus to be recessive or irregularly dominant. The hereditary weakness need not manifest itself until the stresses of life have increased materially, just as in the case of certain types of hernia, some aneurysms and probably some esophageal dilatations.

Endocrine dysfunctions involving the pituitary, the thyroid and the gonads have been suggested as causes. One may conjecture on a possible etiologic factor in relaxin, a substance derived from the corpus luteum in early pregnancy.

Alterations of metabolism and avitaminosis have also been mentioned repeatedly as important etiologic factors.

One should consider the possibility of elastic tissue degeneration as the cause, analogous possibly to the formation of striae gravidum, pseudoxanthoma elasticum and even pinguecula.

Apparently nothing is known concerning the early pathologic changes. The few pathologic reports available, including the ones in this paper, concern only late stages in which complications and sequelae are numerous. There appears to be little inherent tendency to repair except in instances of sudden increase in conicity with or without acute hydrops of the cornea or perforation.

Experimental attempts to determine how much stretching the cornea can withstand were made by means of a Scott tester.

Review of the literature on pressure treatment of keratoconus shows that it has been tried for many years, but few suggest prolonged use of considerable pressure. Our experience has shown that pressure applied for ten weeks or longer may cure the deformity. The cornea thickens and produces a relatively dense corneal scar, usually of an amount somewhat less than that obtained after cauterization. The pressure must be maintained long enough to permit the newly developing scar tissue to attain sufficient strength to hold the cornea in its normal curve. This treatment at present is not recommended for all patients with keratoconus. When it is administered, care must be taken to watch for the complications of iritis, vascularization of the cornea and loss of substance with erosion of the corneal surface. Some of the results are startling, both for reduction of the deformity and for improvement of vision. If the scar formation is dense and large, iridectomy, or better, a corneal transplant opens up further hope of improvement.

DISCUSSION

Dr. Frederick H. Verhoeff, Boston: I have a question from Dr. Arthur Alexander Knapp: "If you have treated keratoconus with vitamin D complex, would you please contrast the results with those of pressure therapy, stressing the early and expected late complications?"

Dr. T. L. Terry, Boston: In the more detailed report of the cases, omitted in reading the paper because of time limitations, Dr. Knapp will see that vitamin A and D as well as calcium were prescribed for all patients following the publication of his reports. It is interesting to note that acute ectasia with hydrops of the cornea developed in 1 patient (case 7) during this therapy. In another patient (case 6) the local physician directed the patient to follow a diet low in calcium when study of the blood chemistry revealed a reduced calcium content. About five days later acute ectasia developed. The contradictory evidence in these cases leaves the question of the value of vitamins A and D and calcium quite open, yet it is our practice to continue the treatment suggested by Dr. Knapp.

Dr. Harry S. Gradle, Chicago: Dr. Olga Sitchevska wishes to ask Dr. Terry if he has studied the effect of the contact glass on the curvature of the cornea.

Dr. T. L. Terry, Boston: Soon after Heine made the statement that the contact glass had a curative effect on keratoconus by splinting the cone, I had occasion to use a contact glass on 2 patients. At this time, early in the days of the contact glass, raised corneal segments were not available. The conicity increased in spite of the glass. The corneas came in contact with the posterior surface of the glass, and in each

instance the cornea became widely vascularized, with the vessels entering the pupillary area.

From the experience in those 2 cases, I believe that one should not consider the contact glass as a good splint or truss to prevent the progress of keratoconus, much less to reduce the deformity. I do not believe that the wearing of a contact glass will have any beneficial effect in reducing keratoconus or in preventing it from increasing unless the cone is touching the glass, a condition to be avoided.

DR. JONAS S. FRIEDENWALD, Baltimore: Dr. Terry spoke of the effect of the pressure bandage as changing the balance between intraocular and extraocular pressure in the sense of producing a relative reduction of intraocular pressure.

At another point in his discussion he said that the effect that he was producing was similar to that of occluding the vortex veins and raising the intraocular pressure. I should like to know whether he has any definite evidence as to the effect of this procedure on the balance of intraocular and extraocular pressure.

In connection with this, he raised the question of miosis in these patients, and I should like to ask whether miosis that fails to respond to atropine but reacts promptly to epinephrine does not indicate a postganglionic paresis of the sympathetic nervous system.

DR. T. L. TERRY, Boston: That pressure treatment does apparently reduce intraocular pressure is based on the fact that palpation of the eye after the pressure bandage is removed shows the eye to be mushy soft in almost every instance.

In the instance in which the needle was inserted into the conjunctiva to see if the eye moved freely under the pressure, the bandage was left on for fifteen minutes. The intraocular tension, measured by means of a Schiötz tonometer, was found to be reduced from 16 mm. to 8 mm. of mercury in fifteen minutes. Of course, that does not mean that while the pressure bandage was on that intraocular tension was lower than normal; it means that after the pressure bandage was removed the intraocular tension was lower.

One actually does not know what the tension in the eye is when the pressure bandage is on. I feel reasonably sure that the pressure bandage immediately produces an increased intraocular tension. The physicochemical mechanism responsible for the balance of intraocular tension will get rid of enough intraocular fluids for the pressure equilibrium of the eye to reestablish its usual balance, and then when the pressure bandage is taken off the end result is an unusually soft eye.

Obstruction of the vortex veins in the healthy rabbit eye leads to a temporary experimental glaucoma, the glaucoma disappearing when collateral circulation has been established. When the vortex veins have been tied, miosis is rather prompt, apparently a manifestation of the intense passive congestion of the entire uvea.

In a person who might already have a tendency to glaucoma, this pressure treatment might precipitate an attack—a reason why the treatment should not be entered into lightly.

Mention of vortex veins was made because it is the only basis by which I felt I could show an analogy between this miosis which was reducible by epinephrine and not by atropine. It is possible that the

miosis may be related to injury to the sympathetic nerve. I discussed that problem with Dr. Adler, and he failed to be impressed as to the plausibility of postganglionic paresis having anything to do with this condition. His reply made me feel that it would not be of any advantage to bring this point up and discuss it when the paper by Scheie and Adler on "The Site of the Disturbance of Tonic Pupils (Adie's Syndrome)" was given last week at the American Ophthalmological Society meeting at Hot Springs, Va. Sufficient data have not been collected in the cases studied to know all of the behavior of the sphincter and dilator pupillae muscles under various miotics and mydriatics necessary to solve this problem fully.

Effect of Certain Physical and Chemical Stimuli on the Caliber of the Retinal Blood Vessels in Man. DR. IRVING PUNTENNEY, Chicago.

Little is known concerning the mechanism of spasm and physiologic constriction of the retinal blood vessels. To study such reactions, it is of the utmost importance to remember that a delicate adjustment or equilibrium exists between changes in the volume pressure of the vessels and the intraocular tension. All known therapeutic measures produce a change in the level of this equilibrium, and this change is usually so complex that the drop in blood pressure or increased intraocular pressure completely overshadows vasodilatation. This has been demonstrated in the accumulated results of recent laboratory investigations by Lambert, Riser, Couadau and Meriel, and Puntenney, and clinicians have been challenged to offer substantial proof that vasodilators actually produce an increase in the caliber of the retinal blood vessels. It is the purpose of this paper to present certain studies made on the caliber of the retinal blood vessels in man and to offer photographic proof of the reactions which were observed.

The technical difficulties associated with this problem in photography were partially solved by adapting the Leica camera with its reflex housing attachment to the Nordenson fundus camera. This facilitated the speed at which consecutive pictures could be taken, and good enlargements were secured by a combination of plenachrome film, Champlin no. 15 fine grain developer and condenser enlarging.

The experimental work was divided into two groups. In the first the effect of reduced intraocular tension was studied by lowering the intraocular pressure with the Kukan apparatus. The only measurable effect was a slight dilatation of the retinal veins. In the second group of experiments the results of amyl nitrite, acetylbetamethylcholine (mecholyl), epinephrine, pentobarbital sodium, hyperpyrexia and cold pressor tests were studied. Measurable dilatation of the veins was recorded in several cases with acetylbetamethylcholine.

DISCUSSION

DR. FREDERICK H. VERHOEFF, Boston: I should like to ask Dr. Puntenney whether he thinks that the central artery of the retina has any nerve supply to the media.

I should also like to ask him if, in view of his studies, he thinks that there is such a thing as an arteriole spasm, and if so, what causes it.

Dr. Irving Puntenney, Chicago: I do not think that any one has ever proved the existence of vasodilator fibers supplying the media of the central artery of the retina. So far as vasospasm is concerned, I cannot venture further explanation, for unfortunately no one knows the answer to it.

Dr. Frederick H. Verhoeff, Boston: Do you think it really occurs?

Dr. Irving Puntenney, Chicago: Yes, I think that it occurs, because I have seen it. I have not followed it with pictures, which I should like to do some time, but I am convinced that it does occur.

Dr. Frederick H. Verhoeff, Boston: You mean you have observed it come and go?

Dr. Irving Puntenney, Chicago: I have seen the caliber of the vessels vary; I have seen the spasm pass down the vessel, appear at one point, and then appear later at another point, especially in cases of essential hypertension and preeclampsia, in which there was marked spasm of the vessels. I cannot give a good explanation for it.

Some Pharmacologic Experiments on Isolated Segments of Mammalian Iris. Dr. Erick Sachs and Dr. Parker Heath, Detroit.

The work herein reported is essentially a study of the sensitization of the iris muscles to certain drugs, isolated radical and sphinctral strips of albino rabbit iris being employed. The apparatus used has been previously described. Three types of sensitization are recognized:

(a) The "threshold" type, in which the minimal effective dose of a primary drug is lessened by some sensitizing agent (which may be another drug or surgical denervation) but the maximal effect producible is not greater than that evocable by some concentration of the primary drug alone.

(b) The "augmentation" type, in which the primary drug and the sensitizer synergistically produce a greater effect than any concentration of either drug alone will produce.

(c) The "qualitative" type, in which some pretreatment renders the reacting system sensitive to some drug or factor to which it would not otherwise respond at all.

A dose of epinephrine was found which would cause a maximal contraction without so damaging the muscle that it would not, after washing, contract equally to a repetition of the same dose. This dose (1 : 500,000 to 1 : 333,333) was designated the "maximally effective concentration" (M. E. C.). The amplitude of contraction of dilator strips loaded with 20 mg. or 140 mg. was determined with the maximally effective concentration appropriate to each load. The ratio of the two amplitudes was taken as an index of the work capacity of the dilator-epinephrine system. The percentage of contractions is not measurable, since the true condition of the "relaxed" muscle cannot be known in the case of any smooth muscle. After treatment with cocaine (1 : 500,000) the strip contracted further to submaximally effective concentration of epinephrine than to the same dose of epinephrine alone. No contraction greater than that to the maximally effective concentration (without

cocaine) could be obtained. It made no difference which drug was applied first. Since the work capacity of the muscle was not increased, the cocaine sensitization of the dilator to epinephrine is clearly of the "threshold" type.

The action of acetylcholine and physostigmine salicylate on sphinctral strips was studied. Each alone is such a powerful stimulator that when acting synergistically neither can be designated as "primary" or "sensitizing." Their mutual sensitization of the sphincter is of the "augmentation" type, since both maximally effective and submaximally effective concentrations of these drugs, used together, evoked greater contractions under either 20 mg. or 140 mg. loads than a maximally effective concentration of either drug alone under the same load. The effect was much greater if the physostigmine salicylate was administered first than if the acetylcholine was used as the "sensitizer."

Fourteen to twenty days after excision of one superior cervical ganglion, the resultant sensitization to drugs was studied; homolateral dilator strips were compared with those from the heterolateral eye as controls. Dilator mounts from the side operated on exhibited a lowered threshold to epinephrine. Thus, sensitization of the dilation of the pupil by the ganglionectomy involves a sensitization of the dilator itself, though, of course, other elements in the whole neuromuscular pattern may be affected as well.

With the loads used, a considerable contraction of the isolated dilator to acetylcholine, and some response also to physostigmine salicylate, was found. The doses were the higher ones among those employed in experiments on the sphincter. Such high concentrations as used by Velhagen in his elicitation of this paradoxic effect were not found to be necessary. Strips from both the side that had been operated on and the other side responded. While the threshold of sensitivity to acetylcholine was about the same in both, the amplitude of contraction appeared to be higher in tissue from the denervated side. It was found that acetylcholine and physostigmine salicylate have mutually augmentative actions on the dilator—an apparently unique demonstration of augmentative sensitization in an adrenergic system. In contrast to the behavior of the sphincter, reversed order of application of the drugs made no difference. The imitation of a cholinergic system by the adrenergic dilator system extends even to a manifestation of a relaxing effect from atropine.

While the dilator is undergoing contraction to acetylcholine and physostigmine salicylate, it is still sensitive to epinephrine and contracts still further when the latter is applied, thus exhibiting a combination of adrenergic and cholinergic properties. A (tentative) conclusion from our experiments may be drawn that there are no strictly cholinergic or adrenergic systems but that any apparent specificity is due to some mechanism which regulates relative thresholds and thus simulates qualitative specificity.

Passage of Horse Serum from the Blood Stream Into the Aqueous Humor of Normal and of Immunized Animals. DR. LOREN GUY, New York.

A study was made of several factors that might influence the passage of an antigen (horse serum) from the blood stream into the aqueous.

The influence of various quantities of horse serum in the blood stream was noted to bear a direct relation between concentration of horse serum in the circulation and penetration into the anterior chamber in normal rabbits.

A local injection of horse serum into the anterior chamber of an eye, prior to intravenous injection, was found to reduce to approximately one-half the threshold for horse serum from the blood into the aqueous.

Since no anti-horse-serum precipitins were found in the aqueous or blood in animals given local injections of horse serum, rabbits in which precipitins were produced by intravenous injection were studied. The threshold was reduced more markedly when precipitins were present than when there was only local injection into the aqueous.

The contralateral eye reacted in the same manner, though less intensely than the inoculated eye, showing a similarity in the immunologic reactions of the two eyes.

DISCUSSION

Dr. Frederick H. Verhoeff, Boston: I should like to ask Dr. Guy if he would not expect a certain slight allergic reaction in the eye which would be associated with dilatation of the blood vessels; and while this might not account for the blood serum coming into the eye, I should think that possibly if in those animals into which he had injected the beef serum he had injected both beef serum and horse serum and found that only the beef serum got into the eye, the possibility that I am speaking of would be excluded.

Dr. Loren Guy, New York: Anything I could say along that line would be purely speculative. The veins are dilated in the rabbits according to Seegal's phenomenon. They are also dilated in any animal receiving 2 cc. of whole horse serum, though not so greatly, and associated with that dilatation there is an increase in the body temperature from two to three weeks.

Dr. Frederick H. Verhoeff, Boston: Would not that explain why horse serum was found in the eye in those animals and not in the eyes of controls?

Dr. Loren Guy, New York: I have no explanation for that.

Dr. Frederick H. Verhoeff, Boston: If an eye is inflamed in any way and becomes congested, the serum will go into the eye most freely, will it not?

Dr. Loren Guy, New York: Yes.

Dr. Frederick H. Verhoeff, Boston: Why would that not account for your result?

Dr. Loren Guy, New York: It might.

Dr. Frederick H. Verhoeff, Boston: Is not that just the explanation you gave?

Dr. Loren Guy, New York: I did not give any.

Dr. Frederick H. Verhoeff, Boston: I thought you said that the reaction was due to precipitants.

Dr. Loren Guy, New York: It might be due to antibody antigen reaction that causes a reaction at the site of the first injection. There is

a definite dilatation following the subsequent injection of the same protein as was injected previously, and that might be a factor.

Dr. Frederick H. Verhoeff, Boston: Do you think that if you had injected both beef serum and horse serum only the beef serum would have appeared the second time?

Dr. Loren Guy, New York: I think it would have, but I did not do any experiments along these lines, so I would not like to say.

Dr. Jonas S. Friedenwald, Baltimore: I should like to ask Dr. Guy whether he did any control experiments to prove that the horse serum which he found after previous injection of horse serum into the anterior chamber was not the horse serum he put in there.

Dr. Loren Guy, New York: I do not quite understand your question.

Dr. Jonas S. Friedenwald, Baltimore: You inject some horse serum into the anterior chamber of an animal's eye and then two weeks later you give an intravenous injection of horse serum. How are you sure that the horse serum you find on tapping the aqueous is not a small remnant of what you put in two weeks before?

Dr. Loren Guy, New York: Because I have shown experimentally that the horse serum was out of the body in thirty-six hours.

Cultivation of Conjunctivitis-Producing and Keratitis-Producing Agents on the Chorioallantoic Membrane of the Chick Embryo. Dr. Phillips Thygeson, New York.

In 1931 Woodruff and Goodpasture reported that the virus of fowlpox could be grown on the chorioallantois of the developing chick embryo and that proliferative lesions containing typical inclusion bodies were produced. Since then a large number of viruses have been grown on the membrane, and the method has found wide application in research on viruses. More recently Goodpasture and Anderson have adapted it to the investigation of bacteria, and the membrane has been used in the study of the meningococcus, the gonococcus, Staphylococcus aureus and other micro-organisms. In an effort to determine the value of the egg membrane method in the cultivation and study of the conjunctival and corneal pathogens, a large number of transfers of exudate from cases of conjunctivitis and keratitis were transferred to the membrane, with the following results:

1. The majority of the bacterial agents of conjunctivitis and keratitis grew well. Exceptions were the agents of streptothricosis and of fusospirochetal disease (Vincent).

2. The Diplobacillus of Morax and Axenfeld, an organism often difficult to cultivate, grew luxuriantly on the membrane.

3. The viruses of vaccinia and of herpes simplex produced characteristic proliferative lesions, but the viruses of trachoma, inclusion blennorrhea and lymphogranuloma venereum failed to multiply.

4. Material from conjunctivitis probably infectious in nature but of unknown etiology, such as pemphigus, acute follicular conjunctivitis (Beal), chronic follicular conjunctivitis, etc., failed to induce lesions of the membrane.

The egg membrane cultures would appear to have particular application in the study of herpes simplex and vaccinia and in suspected diplobacillary conjunctivitis when ordinary culture methods have failed.

A Comparative Study of the Effects of Acetylbetamethylcholine, Carbaminoylcholine, Physostigmine Salicylate, Pilocarpine, Atropine and Epinephrine on the Blood-Aqueous Barrier. DR. KENNETH C. SWAN and WILLIAM M. HART, M.S., Iowa City.

Certain clinical effects of the autonomic drugs have been attributed to alterations in the blood-aqueous barrier. Comparative studies were made of the effects on this barrier of atropine, physostigmine salicylate, pilocarpine, epinephrine and two relatively new drugs, acetylbetamethylcholine (mecholyl) and carbaminoylcholine (doryl). In addition, the effects of physiologic variations in pupillary size were investigated.

In previous studies emphasis has been placed on increased protein content of the aqueous as an indication of increased permeability of the barrier between the blood and the aqueous. However, the concentration of proteins or other solutes in the aqueous might be increased or decreased either by alterations in the ocular water balance or altered metabolism of the intraocular tissues.

Variations in the time required for certain crystalloid dye substances to pass from the blood into the aqueous also have been used as criteria for detecting increased or decreased permeability of the blood-aqueous barrier. However, the passage of these readily diffusible substances into the aqueous is dependent on the size of the intraocular vascular bed and on the total blood flow through the eye as well as on permeability of the blood-aqueous barrier. In addition, the passage of dyes through the stroma of the ciliary body has been shown to be affected by their electric charge and toxicity.

Studies with the use of a substance the entrance of which into the eye is dependent only on molecular size have not been reported. Such a test substance should be nontoxic, chemically inert in tissue fluids, osmotically inactive in the concentrations used, without electric charge, suitable for microanalysis and slightly larger than the threshold size for passage into the normal eye from the blood. A polysaccharide, purified dahlia inulin, was found to meet all of the requirements. This substance has been used extensively in filtration studies on the glomerulus of the kidney, but its special properties have not been utilized in ocular investigation.

The effects of the various drugs on the passage of inulin from the blood into the aqueous of rabbit eyes were determined. To provide confirmatory evidence, the concentration of solutes in the aqueous and the time required for certain fluorescent crystalloid dyes to pass into the aqueous were studied. Chemical analyses were made on the aqueous of over 600 rabbit eyes. In addition, 200 rabbits were used in the dye studies. The results are tabulated and discussed.

Mucopolysaccharide Acid of the Cornea and Its Enzymatic Hydrolysis. DR. KARL MEYER and ELEANOR CHAFFEE, New York.

The nature of the corneal mucin has been much debated, and no adequate data have yet been published to establish the nature of the carbohydrate moiety of this corneal fraction.

We have isolated from beef cornea a sulfate-containing mucopolysaccharide acid composed of 1 mol each of hexosamine, uronic acid. acetyl and sulfuric acid, i. e., a substance having the composition of a mucoitin-sulfuric acid in the terminology of Levene. Previously a substance of the same composition had been isolated in our laboratory from pig gastric mucosa, and from both the cornea and the gastric polysaccharides, glucosamine had been isolated. However, the two substances are quite distinct, the main differences being in their rotation and enzymatic hydrolysis. We have found two enzymes which hydrolyze the corneal polysaccharide but which are completely inactive against the gastric polysaccharide. One enzyme is derived from pneumococci, and the other from testis extracts containing the "spreading factor" of Duran and Reynals. By this hydrolysis and by its rotation, the corneal polysaccharide is characterized as the monosulfuric acid ester of hyaluronic acid. The corneal polysaccharide apparently occurs only in the substantia propria, since only this layer gives the metachromatic staining with toluidine blue characteristic of sulfuric acid esters.

Two problems of clinical interest are now being studied: (1) the possible role of the polysaccharide-splitting enzyme produced by pneumococci and by certain group A streptococci (three) in the production of corneal ulcer and (2) a possible relation between the polysaccharide and the maintenance of corneal transparency.

DISCUSSION

DR. FREDERICK H. VERHOEFF, Boston: I should like to ask Dr. Meyer if the stroma of the sclera gives the same sort of staining that the cornea does.

DR. KARL MEYER, New York: In the article by Jorpes, Holmgren and Wilander, which I mentioned earlier in the paper, the statement is made that the sclera of man shows no signs of any metachromasia. In bovine sclera the authors find some scattered "mast cells" which show metachromatic granules. They claim that these "mast cells" carry heparin, which as a carbohydrate polysulfuric acid ester strongly takes the metachromatic stain. The work of the Swedish authors was undertaken to test for the origin and occurrence of heparin. We have tested the cornea polysaccharide for activity of heparin and found it weakly active. Furthermore, heparin is completely resistant against our enzymes. so that we are certain we were not dealing with heparin.

Dark Adaptation and Dietary Deficiency in Vitamin A. DR. LINCOLN
F. STEFFENS, DR. HUGO L. BAIR and CHARLES SHEARD, PH.D..
Rochester, Minn.

Investigations concerning the effects of dietary deficiency in vitamin A on dark adaptation were undertaken because of the various criticisms which have been offered regarding experimental ensembles and technics and because of the disparity of the findings obtained and the conclusions reached.

In 3 normal adult subjects, the thresholds of light intensity and courses of dark adaptation of the macular areas and of regions 10 degrees above the macula were not affected significantly (less than 0.5 log

unit) during the course of a dietary regimen very low in content of vitamin A (100 to 300 international units daily) for periods of forty-four, one hundred and sixty and one hundred and eighty-nine days respectively. These experimental results were checked and corroborated by tests made with different intensities of and exposures to the light-adapting field (160 to 1500 millilamberts) and with retinal stimulus areas of 0.33, 1 and 2 degrees respectively. Other types of apparatus for photometric measurement of visual adaptation gave comparable data. The results we have obtained show that in certain normal persons considerable periods of deficiency in the intake of vitamin A may be maintained without producing any significant changes in dark adaptation for either rods or cones. In contrast, however, microscopic examination of the skin of one of the subjects (on a diet low in vitamin A for one hundred and eighty-nine days) showed the presence of changes (hyperkeratosis, keratotic plugging of hair follicles, etc.) which it is believed generally occur in the last stages of avitaminosis A. Restoration to a normal cutaneous condition, except for occasional keratotic plugs in the hair follicles, occurred in about three weeks on normal diets supplemented with a fairly large (80,000 units) daily intake of vitamin A.

Measurements of dark adaptation have been made in conditions of follicular hyperkeratosis and in clinical cases of persons reporting restricted diets and diets low in vitamins for prolonged periods. In general, threshold levels are above normal in these conditions: Diets high in vitamins cause partial or complete restoration to normal ranges of dark adaptation, although there are marked differences in the periods of time required to produce significant changes in threshold levels.

DISCUSSION

DR. JONAS S. FRIEDENWALD, Baltimore: Dr. Joseph Mandelbaum asks this question.

"In view of the results obtained on a vitamin A deficiency diet by Jeghers, Wald, Adler and McDonald, Booher and Callison, and Hecht and Mandelbaum—the last of whom have observed 17 cases—do you not think that these results are the exception rather than the rule? How do you explain this?"

DR. LINCOLN F. STEFFENS, Rochester, Minn.: Of course it is possible that these results may be an exception that we are reporting. However, there were three of us on the same diet, and all of us came from different sections of the nation. The "thresholds" remained at approximately the same level in each case during the period of dietary deficiency. We think that the discrepancy between the findings of various investigators may be explained by a variation in the ability of different persons to store vitamin A, although we have no experimental evidence to prove it.

DR. FREDERICK H. VERHOEFF, Boston: Dr. Arthur Alexander Knapp asks this question: "Since vitamin D has been reported to be of value in dark adaptation, may I ask if you have any comparative results with vitamin A?"

DR. LINCOLN STEFFENS, Rochester, Minn.: No, we have not. During our period of dietary deficiency, each experimental subject has a

daily intake of 15 drops of irradiated viosterol. The consensus at that time was that our dietary requirement was very adequate in vitamin D content, and therefore we have no information to contribute to answer that question.

DR. EDWARD JACKSON: In recent articles in the English literature, in London, there has been proposed that light and dark adaptation should be taken as a test of vitamin A sufficiency or insufficiency. However, this applied to, and instances cited were entirely among, school children, generally of the early years of school life and in the stratum of society where poor general nutrition was likely to be. Have you made any investigation with reference to the liability of interference with light adaptation in children as compared with adults?

DR. LINCOLN F. STEFFENS: Yes, Dr. Jackson, that is being done now. Some work has been finished, but there is a group of doctors at the Mayo Clinic who have already examined a large number of children in the city of Rochester, Minn., and they have been unable to detect any evidence of vitamin A deficiency in any of them. An experimental diet is not being used in this investigation.

Book Reviews

Cardiovascular-Renal Disease. By Lawrence W. Smith, M.D.; Edward Weiss, M.D.; Walter I. Lillie, M.D.; Frank W. Kronzelmann, M.D., and Edwin S. Gault, M.D., Philadelphia. Price, $4.50. Pp. 227, with 75 illustrations and a number of plates in colors. New York: D. Appleton-Century Company, Inc., 1940.

This book presents a clinicopathologic correlation study emphasizing the importance of ophthalmoscopy and is based on material exhibited at the eighty-ninth annual session of the American Medical Association in San Francisco in 1938. This exhibit received the Frank Billings' Gold Medal. The study is the combined work of the departments of pathology (Smith, Kronzelmann and Gault), of medicine (Weiss) and of ophthalmology (Lillie) at Temple University, Philadelphia.

This correlation of available information on cardiovascular-renal disease must be greeted as a step forward and in the right direction and as a means of advancing the knowledge of important problems in medicine. It emphasizes the close relation between the various branches of medicine, a point which cannot be too often insisted on. It is fortunate that at Temple University a group was found interested enough to work out this problem.

The subject matter is considered under the following chapter headings: I, "Hypertensive Cardiovascular-Renal Disease," II, "Essential Hypertension (Nephrosclerosis)," III, "Senile Atherosclerosis (Arteriosclerosis)," IV, "Nephritis," V, "Nephrosis" and, VI, "Clinicopathological Consideration," followed by appendixes and a bibliography.

There is no more important ophthalmoscopic study than the proper recognition of vascular disturbances of the retinal vessels and their significance in general diseases. These are admirably described in this book, as are also the microscopic and clinical lesions of the underlying factors in general disease.

The authors deserve great credit for the lucid description of the subject matter and for the excellent illustrations, not only of histologic changes but of the lesions of the fundus. An excellent introduction to vascular ophthalmoscopic changes will be found in chapter II, illustrated with colored drawings. In each chapter a characteristic clinical case is completely described, and the associated ocular changes are illustrated by a photograph of the fundus and a description of the ophthalmoscopic findings. A complete bibliography concludes the volume.

This is a most instructive and excellent treatise which will be invaluable to any one interested in medical ophthalmology. The illustrations could not be improved on. The authors and publishers deserve credit.   ARNOLD KNAPP.

Les aspects normaux et les anomalies congénitales du fond de l'oeil. By Marcel Danis. Pp. 193, with 104 illustrations and 38 colored plates. Paris: Masson & Cie, 1940.

This is the twelfth in the series of monographs published under the auspices of the Société française d'ophtalmologie.

The first chapter deals with the history of ophthalmoscopy, beginning with the observations on the fundus reflex made by Aristotle and Pliny and ending with the revolutionary developments following the work of Helmholtz. The chapter on the ophthalmoscope is also largely historical, but in addition it includes descriptions of the most modern instruments and technics. Filtered, red-free and polarized illuminations are discussed, and methods of retinal photography are described. Two short chapters are devoted to a résumé of the anatomy and embryology of the eye.

The author's classification of developmental anomalies as fissural or nonfissural is necessarily incomplete and often confusing. For example, he lists colobomas of the optic nerve under "fissural anomalies." Fifty pages later, after having read about many other anomalies, including the numerous abnormalities of the blood vessels, the reader finds himself dealing again with the optic nerve, this time with anomalies which are nonfissural in origin. Similarly, 60 pages separate colobomas of the macula from variations in foveal position, size, shape and reflex.

Additional chapters deal with pigmentary anomalies and the fundus in ametropia and senility. The chapter on the eye in death (which may be normal but certainly is not congenital) might perhaps have been omitted.

Generally speaking, the book suffers from faulty emphasis. For instance, there are more than 20 pages of history but only 4 pages devoted to pigmentary anomalies.

The black and white illustrations, taken largely from other works, are instructive, but the colored plates are routine and disappointing.

However, the bibliography is excellent, and the book will serve as a guide toward a fuller knowledge of congenital anomalies of the ocular fundus.

G. M. Bruce.

Proceedings of the All-India Ophthalmological Society. Volume VI. 1938 session. Pp. 243, with 8 plates. Madras: Madras Publishing House, Ltd., 1939.

The annual meeting of the All-India Ophthalmological Society was held at Bombay on December 19 to 21, 1938, at the Grant Medical College, Bombay. After an address of welcome by Lieut.-Col. Sir J. N. Duggan, O. B. E., the presidential address was delivered by Dr. S. N. Kaul, who spoke on the prevention of blindness. The principal topic of the congress was a symposium on uveitis. A number of papers on clinical observations were presented. Among these may be mentioned papers entitled: "Recurrent Hemorrhage in Retina and Vitreous in the Young Adults," "Treatment of Bengal Glaucoma," "Surgical Treatment of Detachment of the Retina," "Treatment of Herpes Zoster Ophthalmicus," "Snake Venom and Its Use in Ophthalmology" and "The Use of Sulfanilamide in Certain Ophthalmic Conditions."

Arnold Knapp.

Directory of Ophthalmologic Societies *

INTERNATIONAL

INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

BRITISH MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

CHINESE OPHTHALMOLOGY SOCIETY

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

GERMAN OPHTHALMOLOGICAL SOCIETY

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

MIDLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

North of England Ophthalmological Society

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.
Place: Perth, Western Australia. Time: Sept. 2 and 7, 1940.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

Sociedade de Ophtalmologia e Oto-Rhino-Laryngologia da Bahia

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

Società Oftalmologica Italiana

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Illl tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Albert C. Snell, 53 S. Fitzhugh St., Rochester, N. Y.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank E. Brawley, 30 N. Michigan Ave., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Place: Cleveland. Time: Oct. 6-11, 1940.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. F. P. Calhoun, 478 Peachtree St. N. E., Atlanta, Ga.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. W. H. Lowry, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.
Place: Chateau Laurier, Ottawa. Time: Oct. 18-19, 1940.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President-Emeritus: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.
Executive Director: Mrs. Eleanor Brown Merrill, 50 W. 50th St., New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. G. Nadeau, 122 E. Walnut St., Green Bay.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Green Bay. Time: October 1940.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles, Calif.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence W. Shannon, 4th and Pike Bldg., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1215–4th Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. W. E. Rideout, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

Sioux Valley Eye and Ear Academy

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. Dake Biddle, 123 S. Stone Ave., Tucson, Ariz.
Secretary: Dr. A. E. Cruthirds, 15 E. Monroe St., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. J. K. Heckert, 103 N. Washington St., Lansing.
Secretary-Treasurer: Dr. W. D. Irwin, 710 Hanselman Bldg., Kalamazoo.
Time: Third Thursday of alternate months.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Hugh B. Barclay, 111 S. Main St., Greensburg.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

Colorado Ophthalmological Society

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. W. E. McClellan, 750 Main St., Hartford.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia
President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.
Place: Macon.   Time: May 13-17, 1941.

Indiana Academy of Ophthalmology and Oto-Laryngology
President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick.   Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology
President: Dr. J. K. Von Lackum, 117–3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.
Place: Cedar Rapids.   Time: November 1940.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society
President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology
and Otolaryngology
Chairman: Dr. O. B. McGillicuddy, 124 W. Allegan St., Lansing.
Secretary: Dr. R. G. Laird, 116 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology
President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology
President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

Nebraska Academy of Ophthalmology and Otolaryngology
President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology,
Otology and Rhinolaryngology
Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.
Place: Atlantic City.   Time: June 3-5, 1941.

New York State Medical Society, Eye, Ear, Nose and Throat Section
Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

North Carolina Eye, Ear, Nose and Throat Society
President: Dr. A. G. Woodward, 100 S. James St., Goldsboro.
Secretary-Treasurer: Dr. M. R. Gibson, Professional Bldg., Raleigh.

North Dakota Academy of Ophthalmology and Oto-Laryngology
President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology
President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland.   Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. W. Carpenter, 200 E. North St., Greenville.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.
Place: Columbia. Time: Nov. 5, 1940.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. J. W. Ward, 2607½ Lee St., Greenville.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.
Place: Fort Worth. Time: Dec. 13-14, 1940.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. A. E. Callaghan, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. George G. Hawkins, Newport News.
Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.
Secretary: Dr. Luther Wilson, Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Richard Gamble, 30 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI OPHTHALMIC CLUB

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGIC CLUB

Chairman: Dr. Albert D. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. J. Charles Dickson, 1617 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. J. M. Masters, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m.; second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President: Dr. Leonard C. Whiting, 121 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Algernon Reese, 73 E. 71st St., New York.
Secretary: Dr. Brittain Payne, 35 E. 70th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President Dr. Morris Davidson, 80 Centre St., New York.
Secretary: Dr. Benjamin Esterman, 515 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. W. Howard Heine, 635 N. Main St., Fremont, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Edward A. Weisser, 119–5th Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Edwin S. Ingersoll, 26 S. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 8 p. m., second Wednesday of each month from September to May.

St. Louis Ophthalmic Society

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Matthew Hosmer, 384 Post St., San Francisco.
Secretary: Dr. Fred Boyle, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. F. R. Webster, State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. John R. Myers, State Tower Bldg., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Frank Costenbader, 1726 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. L. Conner Moss, 1710 Rhode Island Ave. N.W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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